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SUMMARY OF RECENT ABSTRACTS*

VII. HELMINTHIASIS

TREMATODES

Schistosomes: General

Distribution.—DE MEILLON (p. 190) discusses the general subject of schistosomiasis in the Union of South Africa. *S. haematobium* has been there for many years, but *S. mansoni* was introduced recently from the north, and is spreading. He gives a list of the snail hosts of these worms, and makes the point that if the rivers of South Africa are dammed for industrial purposes they will become suitable for the breeding of snails. The immigration and settlement of large numbers of people from neighbouring countries, many of whom are infected, will tend to spread the disease unless adequate measures are taken to prevent it.

WILKINS (p. 443) writes of schistosomiasis in S. Rhodesia, where in Africans infection rates of 30 per cent. for *S. haematobium* and 8 per cent. for *S. mansoni* were found after a single examination of many thousands of specimens. He thinks that so many people are infected that treatment alone cannot cope with the situation, and he describes the methods he has found useful for killing snails in quiet rivers, ditches and canals, by means of copper sulphate. In comment, ALVES points out that the method can hardly be applied to rivers with broken and irregular banks. GELFAND (p. 796) refers to the very heavy rates of infection found in the Africans of Mashonaland, and to the late sequelae and complications of schistosomiasis. Details should be sought in the original.

Schistosomiasis is common in Nyasaland and *S. haematobium* eggs were found by RANSFORD (p. 618) in 50–80 per cent. of urines of those in Kota Kota hospital or living on the lake shore; *S. mansoni* eggs were found in about 1 per cent. of specimens of faeces, a reduction from the 7 per cent. of 10 years earlier. The only snail found infected was *Physopsis globosa*. The author discusses the habitat of this snail, and the use of drainage, and of *Tephrosia vogelii*, in controlling the snail host.

LOVETT-CAMPBELL (p. 793) shows that *S. haematobium*, and to a smaller extent *S. mansoni*, were common in West African troops during the war, and that infected soldiers soon broke down under prolonged stress.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1948, v. 45. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

SCHWETZ (p. 348) has written a monograph on the classification and nomenclature of the Planorbidae, especially of the Belgian Congo. This is a very difficult family, and the author advises that specimens taken in the field should be submitted to leading malacologists for identification.

COWPER (p. 444) makes the point that species of snails which serve as intermediate hosts of schistosomes in certain areas may be insusceptible to the same species of schistosomes in other countries. He gives examples, and concludes that this species-specificity, or even strain-specificity, is important in any " species sanitation " of snails.

WRIGHT (p. 913) has summed up the geographical distribution and snail hosts of *S. haematobium, S. mansoni* and *S. japonicum.*

KERVRAN (p. 445) shows that *Physopsis africana* is the common host of *S. haematobium* in part of the French Sudan, and that it is also found infected with *S. mansoni,* but much more rarely. *Planorbis adowensis* is commonly a host of *S. mansoni* in the same area. He discusses other fresh-water snails investigated.

Hosts.—BOSCARDI (p. 92) has studied the development of *S. haematobium* in the host snails. He shows that the miracidia do not penetrate the skin, but enter by the mouth. He claims that only one miracidium develops in a snail, some sort of immunity seems to prevent invasion by a second miracidium. MALDONADO and ACOSTA MATIENZO (p. 192), on the other hand, give a different account of the process of infection of *Australorbis glabratus* by miracidia of *S. mansoni.* They state that the miracidium penetrates the epidermis and that a snail may be parasitized by numerous miracidia, though not all of these will develop. The authors describe in detail the successive stages of the developing embryo in the tissues of the snail. VON BRAND and FILES (p. 526) have found that infection with *S. mansoni* interferes to some extent with the metabolism of *Australorbis glabratus,* but have not decided whether this effect is due to toxic action of the parasites.

HUNTER *et al.* (p. 349) found that, in various batches of *Oncomelania quadrasi,* the best results were obtained when each snail was exposed to 5–10 miracidia of *S. japonicum* [compare Boscardi above]. A period of about 11 weeks is required for the development of cercariae.

Schistosomes.—CRAM *et al.* (pp. 914, 915) discuss the infection of laboratory animals with the human schistosomes, and YOLLES *et al.* (p. 349) have described a perfusion technique for recovery of schistosomes from laboratory animals.

KREIS (p. 617) has made a contribution in which he discusses the nomenclature of the genus sometimes named *Schistosoma* and sometimes *Bilharzia.* The matter has been referred to the International Commission on Zoological Nomenclature but a ruling has not yet been given.

The survival times of cercariae of *S. japonicum* and *S. mansoni* in water at various temperatures and *p*H values were investigated by JONES and BRADY (p. 916). Survival was possible for 8½ days at 5°C., but for only one minute at 55°C. Slight acidity or alkalinity made no difference. Water-treatment processes were investigated by the same authors (p. 918) for their effects on cercariae of *S. japonicum* and *S. mansoni.* Coagulation was not useful, but filtration through Seitz pads held back the cercariae completely. Certain chlorine compounds showed good effect, and also two iodine compounds provided that not too much organic material was present. Certain other chemicals were also effective.

Miracidia of *S. japonicum* and *S. mansoni* are killed within 30 minutes of chlorination or chloramination to total residuals of 0·2 to 0·6 p.p.m. JONES and HUMMEL (p. 919) show that eggs are more resistant, and are killed in 30 minutes only at total residuals of 3·9 to 11 p.p.m., though longer exposure at lower residuals may be effective.

In a comprehensive investigation of the effect of sewage treatment processes on the eggs of *S. japonicum* JONES *et al.* (p. 917) have shown that sedimentation removes most of the eggs within 2 hours, but that anaerobic sludge digestion, sludge drying, and trickling-filter treatment were not very successful in destroying eggs. Activated sludge is a good medium for the hatching of eggs. Intermittent sand filtration, with sand of a certain size, is an efficient method of removing the eggs from treated sewage.

Clinical findings.—MEESER *et al.* (p. 794) in S. Rhodesia have found that rectal biopsy is much more satisfactory than Weller's scraping method for diagnosis of rectal schistosomiasis, though the latter is of considerable value in Egypt and the Caribbean, where infections are heavy. The intradermal test with the authors' cercarial antigen gave more positive results than rectal biopsy. In S. Rhodesia rectal infection with *S. haematobium* is quite common.

ERFAN and TALAAT (p. 715) have found liver biopsy a simple, safe and useful means of diagnosing hepatic schistosomiasis ; they found eggs of *S. haematobium* or *S. mansoni* in 21 of 41 specimens from cases examined in Egypt.

FAUST (p. 716) has contributed a detailed discussion of the ectopic lesions found in schistosomiasis, which are those produced outside the portal-caval venous blood channels. In 82 cases, 21 were attributable to *S. haematobium*, 12 to *S. mansoni* and 49 to *S. japonicum* ; most of those due to *S. haematobium* were outside the brain, but most of those due to *S. japonicum* were within it. These ectopic lesions can usually be accounted for by the natural, valveless intercommunicating channel between the portal and caval veins. The lesions may develop several years after intestinal or vesical lesions have disappeared.

REEVES and KERR (p. 448) describe a case of infection with *S. japonicum* in which there was a granulomatous tumour of the brain which contained many *S. japonicum* eggs. The tumour was removed and the patient made a good recovery after the operation and after treatment with antimonials. HUNT *et al.* (p. 624) report a case of cerebral schistosomiasis in which the signs were those of cerebral tumour. A nodule which contained eggs of *S. japonicum* was removed from the brain, and under antimony treatment the patient made a good recovery.

RAPER (p. 1017) reports a case in which eggs of *S. mansoni* were found in a brain thrombus, and another in which they were present in a mass of fibrous tissue in the spinal canal, compressing the cord.

AFIFI (p. 718) has written a book on bilharzial cancer, but he points out that there is little or no evidence that the schistosomes are specific causes of cancer. He discusses diagnosis and treatment of cancer associated with schistosomiasis. MAKAR Bey (p. 795) reports two cases of bilharzial papilloma and epithelioma.

LOVERIDGE *et al.* (p. 716) have investigated the educational attainment of European and African children, suffering from schistosomiasis. They found some evidence that the disease had an adverse effect in European children, but there was no such evidence for African children. They discuss the implications of these findings. [See also KIESER, below.]

Treatment.—SCHUBERT (p. 620) sets out the optimum conditions for testing drugs in experimental schistosomiasis of mice. Details should be sought in the original. He (p. 621) reports on over 400 compounds tested under these conditions, and notes that the pentavalent antimonials neostibosan and neostam [used in kala azar] show considerable activity, and also antimony compounds soluble in oil, and Miracil. The best results were obtained with certain new antimony compounds, which are named. He also tried the drugs during the early days of infection, and several showed protective action.

Miracil has been used for the treatment of schistosomiasis ; LATNER *et al.* (p. 96) describe a method for estimating it in biological fluids. Miracil D is

best given by mouth and HAWKING and ROSS (p. 798) found that a dose of 0·2 gm., repeated daily, was tolerated. They studied blood levels and tissue concentrations, and the effects of overdosage in animals. HALAWANI *et al.* (p. 721) have studied the blood levels of Miracil D after oral administration, and recommend that it should be given at intervals of 12 hours. WATSON *et al.* (p. 1018) have used Miracil D in *S. haematobium* and *S. mansoni* infections in Egypt. It is given by the mouth, and toxic effects are slight. It is effective against both worms, but with the doses used, complete cure is not usually obtained. In comment, HAWKING refers to the better results he and his colleagues obtained, with higher doses, in S. Rhodesia. HALAWANI *et al.* (p. 797) have used Miracil D in patients infected with *S. haematobium*, and they conclude that the effective dose is not less than 18–20 mgm. per kgm. daily for 7–8 days; the blood concentration must reach 0·3 mgm. per 100 ml.

LIPPINCOTT *et al.* (p. 527) have studied the distribution and fate of antimony in the body after administration to patients with *S. japonicum* infection. Details should be sought in the original. In tests of white rats after administration of radio-active tartar emetic, NESS *et al.* (p. 447) noted anomalies in distribution of antimony in the blood and tissues, and suggest that if rats are used to screen antimonial compounds, such findings should be interpreted with caution.

GIRGIS and AZIZ (p. 446) have used an intensive 2-day course of injections of sodium antimony tartrate in the treatment of schistosomiasis in Eygpt, and although they report fairly good results, they incline to think this method too drastic for large-scale campaigns. TALAAT and SHOAIB (p. 719) have tried various intensive courses of treatment for schistosomiasis in Egypt, and finally recommend two injections of tartar emetic at intervals of 6 hours, on two consecutive days (a total of 8 grains of the drug). In comment, ALVES points out that certain details are not made clear by the authors.

The question of acquired tolerance to tartar emetic and some other antimonials has been studied by PAK (p. 96). Trivalent and pentavalent antimonials produce tolerance and are not cumulative; the toxicity of tartar emetic is increased if the experimental animals are starved.

As a result of experimental work on monkeys infected with *S. haematobium* SAID EL AYADI (p. 720) concludes that Repodral (Fouadin) is curative if given by the mouth together with riboflavin.

ROSS (p. 619) reports very poor results from the use of acriflavine in the treatment of schistosomiasis.

S. haematobium

GAUD and MAURICE (p. 912) confirm the existence of urinary schistosomiasis in the Wady Sous region of Morocco, but GAUD *et al.* (p. 1015) give evidence that infestation with *S. haematobium* has declined recently in Morocco as a whole.

BOIRON and KOERBER (p. 93) name the endemic areas of *S. haematobium* infection in French West African territories. These are very extensive, the disease being found along the main water-routes. The incidence is probably some 15–20 per cent. in schoolboys and local troops.

GORMAN *et al.* (p. 258) describe a method for hatching out the eggs of *S. haematobium*, and detecting the presence of the miracidia released. It is often important to know if viable eggs are present in urine.

BLAIR and ROSS (p. 1094) describe the antigen they prepare from cercariae emitted by *Physopsis africana* infected in nature; these cercariae may not all be *S. haematobium*, but no claim has ever been made that antigens from cercariae are species-specific. They have followed the course of the reaction after

intradermal injection of this antigen in infected persons, and show that it differs markedly from the course in uninfected persons. The optimum time for reading the tests is 15 minutes after the injection.

Gelfand (p. 913) shows that the ureters are often affected in vesical schistosomiasis in S. Rhodesia; he has found ova in the submucosa and the muscular layers, and notes that the pathological changes lead to dilatation, but he has not seen true stenosis.

Talaat (p. 1093) argues that kidney function is impaired in urinary schistosomiasis and that tartar emetic treatment does not impair the function in the doses normally used.

In the hands of Blair *et al.* (p. 526) Miracil D gave poor results in the treatment of *S. haematobium* infections in S. Rhodesia, but later results were better, see Hawking above.

Kieser (p. 526) comments on the deleterious effect of *S. haematobium* infection on the intelligence and vigour of children in South Africa.

In discussing the control of *S. haematobium* infection in Algeria, Marill (p. 798) makes the point that the disease is largely associated with the irrigation systems, and that although it is not possible to deal with all the large number of snail foci in the country, those in the irrigation canals can be controlled. Engineers should know that snail elimination is an essential part of their work. Canals should be cemented and dried periodically, and copper salts can be used for the parts of the irrigation system which are permanently under water. Similar measures are also useful in malaria control. Blair (p. 1095) discusses the public health aspects of schistosomiasis in S. Rhodesia, where, he thinks, both the urinary and the intestinal forms are spreading. Attack on the worm can be pushed by intensive treatment, and on the snail by the use of copper sulphate and by the planning of irrigation works and water-storage dams with schistosomiasis in mind from the beginning. He makes the point that cercariae can live 100 hours in winter.

Khalil and Halawani (p. 527) do not consider that the preparation known as Cloroben is suitable for use against snails, because it is lethal to fish and rice plants.

S. mansoni

Schwetz and Dartevelle (p. 348) have published a detailed study of intestinal schistosomiasis in the Kasenyi area of the Belgian Congo, in which they show that it is not particularly associated with fishing. The monograph is chiefly concerned with a malacological survey of the area from Lake Kivu to Lake Albert, and a description of the species found. Schwetz (p. 1015) has contributed a long paper on schistosomiasis in the Lubilash area of the Belgian Congo, where the incidence of *S. mansoni* is up to 14 per cent. (50 in one district). It is a disease of cultivators, and may be concerned in some cases of the condition known as *diboba*. He gives a list of the snail vectors.

Heisch (p. 671) reports infection with *S. mansoni* in 11 per cent. of a group of Africans near Taveta, Kenya.

S. mansoni infection is endemic in several places in Eritrea, and Ferro-Luzzi (p. 1017) has found that *Planorbis abyssinicus* and *P. ruppellii* are hosts.

Luttermoser (p. 447) has contributed a comprehensive account of schistosomiasis in Venezuela, where there are probably more than 50,000 cases along the coast and the main drainage systems. The snail host is *Australorbis glabratus* and the author describes the methods used to eradicate it by drainage and the use of copper salts or lime. There is a special risk in connexion with the cultivation of water-cress, sugar-cane and a certain reed which is used for animal packs.

MEIRA (p. 346) has written a long monograph on schistosomiasis in Brazil where it has been estimated that some 3,000,000 people are infected. He thinks that this is probably an under-estimate. In some places the infection rate (on the evidence of examination of faeces) is as high as 56 per cent. in the age group 11–15 years. The snail hosts are *Australorbis glabratus, Planorbis guadeloupensis* and *P. olivaceus.* [Some authorities regard *A. glabratus* as the correct name for *P. guadeloupensis.*] PORTELA (p. 347) gives an even higher figure for infection in Pedra Azul, Brazil, where he found it in 85 per cent. of 1,500 persons of all ages over 2 years. JANSEN (p. 95) shows that infection with *S. mansoni* in part of Pernambuco, Brazil, is present in 6·6 per cent. of children up to 4 years of age [not 40 as in the abstract], and that the proportion rises to 71 per cent. at age 15–24, falling to 35·4 per cent. over 55 years. The snail concerned is *Australorbis centimetralis.* In treatment tartar emetic gave the best results, but other antimonials were also useful. In a survey conducted along the Victoria-Minas railway in Brazil BASSÈRES and PANTOJA (p. 191) found infection with *S. mansoni* in 21 per cent. of the people living near the river Doce, but in only 0·9 per cent. in communities far from that river. Infection of snails (*Planorbis olivaceus*) found in various collections of water showed a similar trend to infection in man. DE MAGALHÃES and ROCHA (p. 618) report on the increasing incidence of *S. mansoni* infection in Minas Gerais, Brazil; in some towns the rate in school children of infection is over 50 per cent.

MONTESTRUC *et al.* (p. 259) show that *S. mansoni* is an important cause of dysentery in Martinique, where *Planorbis guadeloupensis* [see comment above] is the snail host.

ELSDON-DEW (p. 189) has used the zinc sulphate floatation method of Faust for detecting worm eggs in faeces, but though this is useful for hookworm eggs it is not so good for schistosome eggs, which do not float well.

OTTOLINA (p. 915) writes of the value of rectal biopsy in diagnosis of *S. mansoni* infections, by which means many cases negative to stool examination are found to be positive. He (p. 193) shows that if the fragments of tissue obtained by rectal biopsy are immersed in fresh water for a few minutes they become sufficiently transparent to allow schistosome eggs to be seen under the microscope. In this way a diagnosis may be made within a very short time. DA SILVA and COSTA (p. 194) also write of the value of rectal biopsy in simplifying the diagnosis of *S. mansoni* infections.

MARTINEZ-VILLAFAÑE and LANG (p. 1095) have used Neostibosan for *S. mansoni* infections, but without much success.

DA SILVA (p. 95) describes his tests of Stiboplex III, a compound of antimony and iodine, which he has used with some success in the treatment of *S. mansoni* infections of animals, and in four human cases. The drug is given intravenously at intervals of 1–3 days to a total of 10–12 injections.

NOYA BENITEZ (p. 619) writes of the value of splenectomy in hepatic cirrhosis which is a result of *S. mansoni* infection. The operation may relieve portal hypertension if performed before the liver damage is excessive. He gives details of 20 cases in which he removed the spleen for this condition.

VOGEL (p. 93) has investigated hermaphroditism in *S. mansoni,* and notes that male worms which also possess ovaries, tend especially to develop in animals which are not optimum hosts (guineapigs and rabbits) but not in man and monkey. The development of these hermaphrodite males is also stimulated by the absence of a female partner, as in animals infected by male worms only. He discusses the implications of these findings.

CRAM *et al.* (p. 913) have shown that the North American snail *Tropicorbis havanensis* can act as host for *S. mansoni.*

S. japonicum

WRIGHT *et al.* (p. 194) report a survey carried out in Japan. They used a simple sedimentation technique for the examination of faeces, and found infection in 22·6 per cent. of 1,688 school children. More boys than girls were infected, and the rates varied in different places, up to 53·5 per cent. in one. These results are much higher than those reported by the Japanese, and this is probably due to the more efficient examination carried out by the present authors than the single faecal smear used by the Japanese. The snail host is *Oncomelania nosophora*, and infection was found in various collections of these snails, up to 15·8 per cent. in one place.

PESIGAN (p. 622) reports a new focus of schistosomiasis in Luzon, Philippine Islands; the snail *Oncomelania quadrasi* was also found.

ABBOTT (p. 1096) has written a handbook on the medically important molluscs of the Far East, with instructions for identification in the field. He cites five hosts of *S. japonicum*:—*Oncomelania quadrasi. O. formosana, C. nosophora, O. nosophora slateri* and *O. hupensis.*

WARD *et al.* (p. 915) describe their methods of maintaining snails in the laboratory; they exposed certain American snails to *S. japonicum*, but only *Pomatiopsis lapidaria* showed signs of infection, and these were regarded as inconclusive. ABBOTT (p. 1097) describes *Pomatiopsis lapidaria* in detail.

BRACKEN *et al.* (p. 1098) describe the lesions of acute *S. japonicum* infection in man, their findings having been made in men killed in the war in the Philippines. The appearances are very similar to those seen in experimental animals.

HUNTER *et al.* (p. 623) report on trials of 10 techniques for recovering eggs of *S. japonicum* from faeces. They recommend two methods which involve the use of HCl, sodium sulphate, Triton NE and ether, with centrifugation at different stages, but for details the original should be consulted. JAHNES and HODGES (p. 623) use 10 per cent. ethyl alcohol (sp. gr. 0·986) for emulsifying faeces and sedimenting eggs of *S. japonicum*, with success.

Although they detected some value in intradermal tests or complement-fixation tests with antigens from adult *S. mansoni* or (especially) from their cercariae, in *S. japonicum* infections, BOZICEVICH and HOYEM (p. 916) did not think that they were as useful as examination of faeces.

VOGEL and MINNING (p. 196) have studied the effects, on adults and eggs of *S. japonicum*, of tartar emetic, Fouadin and emetine injected into animals infected with that worm. These are described in detail. The first two drugs could effect cure if doses were given 15–18 times, but no cures were obtained with emetine in this series. CARROLL and HUNNINEN (p. 624) treated a series of American soldiers who were infected with *S. japonicum*, by intravenous injections of tartar emetic given every other day. The results were slightly better than with Fouadin.

In a test of a large number of compounds, to find those which would protect against cercariae of *S. japonicum* after clothing had been impregnated with them, WRIGHT *et al.* (p. 527) found that an emulsion of 4·5 per cent. benzyl benzoate with 0·5 per cent. Tween 80 in water was the most effective. Garments impregnated with this, and then dried, protect even after having been washed four times. Dibutyl phthalate emulsion is also useful, and so is a secret gas protective chemical. The type of cloth impregnated is important, wool being better than cotton or twill. The same authors (p. 529) investigated the protective effects of repellents and repellent ointments for application to the skin. Many showed useful effect, but tests are needed to determine the length of time during which these would remain effective on continuous exposure to water. These experiments were conducted during the war. Similar investigations are reported by NOLAN *et al.* (p. 919), who found that dibutyl phthalate

in garments provided protection after they had been rinsed for more than 96 hours, and lasted through five washes in soapy water. One other substance was more protective, but less resistant to the action of soap. Untreated materials, especially woollen serge, afford good mechanical protection.

KUNTZ *et al.* (p. 621) have devised a method of testing ointments and fabrics for effectiveness as barriers to schistosome cercariae, which involves the use of rabbits and the cercariae of *Schistosomatium douthitti*.

ATKINS (p. 1019) suggests that copper soaps may be effective repellents for schistosome cercariae.

Other schistosomes

MCMULLEN and BRACKETT (p. 920) sum up much of their information on schistosome dermatitis in Michigan, noting the areas of prevalence and the snails concerned.

Other trematodes

GONZÁLEZ CASTRO (p. 197) reports a few cases of infection with *Fasciola hepatica* in Spain. KOURI (p. 799) discusses the diagnosis, epidemiology and prevention of human *Fasciola* infection. MANDOUL and PAUTRIZEL (p. 800) show that the mere presence in the faeces of eggs of *F. hepatica*, and of *Dicrocoelium*, is not sure evidence of infection, since eggs ingested in infected sheep liver can be found in the faeces for several days.

GALLIARD and NGU (p. 259) make the point that *Fasciolopsis buski* from human, porcine and canine hosts are of one species only. The geographical distribution is explicable by the food habits of the people of various countries. Some communities make use of the plants on which cysts are formed, others do not. WU (p. 97) finds that guineapigs are not suitable hosts for *Fasciolopsis buski*.

PESIGAN (p. 622) notes that paragonimiasis is to be found in Luzon, Philippine Islands.

The first case of intestinal heterophyidiasis in the Philippines to be diagnosed during life is reported by GUTIERREZ *et al.* (p. 259).

ROCHE (p. 800) found a trematode of the genus *Dicrocoelium* in an intrahepatic bile duct in a human liver in Nigeria. This is the first record from West Africa.

PICK and DESCHIENS (p. 350) describe the clinical course of infection of baboons with *Watsonius watsoni*, and the pathological appearances in some which died. They (p. 800) have published new observations on *Watsonius watsoni*.

CESTODES

TÖTTERMAN (p. 449) states that *D. latum* may cause typical pernicious anaemia, or mild hyperchromic anaemia, but he has seen no true evidence that it can cause hypochromic anaemia.

HIRVONEN (p. 260) discusses the differential diagnosis of pernicious anaemia and severe tapeworm anaemia due to *D. latum*; details should be sought in the original. He (p. 450) thinks that a toxin from *D. latum* has a " paralysing effect on the blood-forming organs, the bone marrow and the liver ", but that anaemia (which, in fact, is rare in persons infested by this worm) is produced as an effect of abnormal worms.

VON BONSDORFF (p. 198) has collected evidence on the site favoured by *D. latum* in the intestine; this indicates that it is most often to be found in the upper small intestine, particularly the ileum. He describes the symptoms in patients who vomit the worm. He (pp. 260, 920) has carried this enquiry further by attempting to find the level at which eggs or proglottides may be found by intestinal intubation. He found that in infested patients with

pernicious type of anaemia the worm was in the jejunum, but that in infested patients without this form of anaemia it was in the ileum. He suggests that if it is high in the intestine it may impair the interaction between the extrinsic and intrinsic factors. He (p. 97) notes that administration of fresh or dried *D. latum* substance does not interfere with the action of extrinsic and intrinsic factors.

ESKOLA (p. 1098) has studied the excretion of urobilin in urine and faeces in relation to *D. latum* anaemia ; for details and discussion of the implications of his findings the original should be consulted.

VARTIAINEN and BASTMAN-HEISKANEN (p. 449) show that dead eggs of *Diphyllobothrium latum* stain well with eosin, but living eggs do not.

ALLEN (p. 97) shows that cysticerci of *T. saginata* are killed by gradual heating to 56°C., but not 55°C. or less. The tissues were placed in water maintained at the temperature desired, and were cooled immediately they reached that temperature.

MAZZOTTI *et al.* (p. 261) describe the symptoms in a large number of cases of tapeworm infestation, and the treatment given. Oleoresin of male fern gave better results than ethereal extract, or pumpkin seeds.

BASNUEVO (p. 1099) gives details of treatment of *T. saginata* infestations with a preparation of tin, for which he claims fairly good results. LE GAC (p. 921) has successfully used tin preparations in the treatment of tapeworm infestations.

GELFAND (p. 721) has studied several cases of cysticercosis of the brain, and of the heart, in Africans of S. Rhodesia. He discusses the clinical symptoms and diagnosis of the condition.

COITO (p. 1019) refers to the prevalence of *Echinococcus granulosus* in dogs in Lisbon, and to human cases of hydatid disease there. Much attention has been paid to hydatid disease in adults, but not so much to its presence in children. MOREY SOTOMAYOR (p. 351) gives an account of 19 cases in children in Peru, five of which were fatal.

LARSH (p. 98) shows that alcohol given to mice infested with *H. nana* var. *fraterna* reduced resistance to development of cysticercoids, probably because in the experiments the alcohol interfered with normal food intake and led to avitaminosis.

OSIMANI (p. 1100) reports infestation with *Dipylidium caninum* in a child.

Charles Wilcocks

[*To be continued*]

MALARIA

CROSNIER, R., MERLE, F. & TABUSSE, L. Paludisme autochtone. [**Indigenous Malaria in France.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 11/12, 681–90. [13 refs.]

The authors describe three cases of malaria in which infection had been acquired in France, one *P. falciparum* and two *P. vivax* infections. One man acquired his infection in the Landes, in Gascony, which in former days was a recognized centre of endemic malaria. The second patient acquired his infection from colonials who had been repatriated from Indochina who were living in close contact with him. The third patient had always lived in the neighbourhood of Paris. There were difficulties of diagnosis in all three cases. *Norman White*

SFORZA, M. Segnalazione del " Plasmodium ovale ", Stephens 1922 in Eritrea. (Nota preventiva). [**Presence of *Plasmodium ovale* in Eritrea. (Preliminary Note).**] *Riv. di Malariologia.* 1948, Dec., v. 27, No. 6, 261–4. English summary (3 lines).

CALLOT, J. Le paludisme en Alsace et en Moselle. A propos d'une enquête récente. [**Recent Inquiry on Malaria in Alsace and in Moselle.**] *Ann. Parasit. Humaine et Comparée.* 1948, v. 23, Nos. 5/6, 289–95, 3 maps.

Alsace was one of the most malarious regions of France in the last century, Even Strasbourg was affected. The endemic had completely disappeared however, by 1885. Inquiries carried out by order of the German government after the annexation of Alsace in 1871 determined the geographical distribution of the disease. The findings as concerns Lower Alsace are recorded on a map. Foci of infection were found along the Rhine including Strasbourg and its environs ; in the marshland bordering the River Ill ; along the River Bruche, and along the Marne-Rhine Canal.

Malaria was also endemic in Moselle until the middle of the last century, notably in the Sarre Valley.

None of the explanations that have been advanced account satisfactorily for the disappearance of malaria about 1885 from both Alsace and Lorraine. The regularization of the course of the Rhine cannot account for it. Stabling cattle in Alsace was practised long before the disappearance of malaria. This practice may well have encouraged the deviation of *A. maculipennis* from man to cattle. *A. m. messeae* is now the predominant species. In Lorraine cattle are not kept in stables.

A certain amount of anxiety was occasioned by the possibility that the introduction of a large number of infected persons into this area during and after the last war might reactivate these old foci of infection. Anophelines are still numerous. The author addressed an inquiry to all medical practitioners in these areas regarding the occurrence of locally acquired malaria infections. From this inquiry it was learnt that though imported cases of malaria had been widely scattered throughout the area, being reported from more than 50 localities in the Lower Rhine area, only two indigenous infections, over and above the few that have been published, had been observed. In these cases races of *Anopheles* theoretically zoophile were responsible for transmission. It would appear that the persistence of anophelism in France need occasion no undue anxiety. *Norman White*

HORMANN, H. Malaria in Deutschland 1945 bis 1947. [**Malaria in Germany, 1945 to 1947.**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. [1949], v. 1, No. 1, 32–91, 27 figs. [Numerous refs.]

This paper deals with the spread of malaria in Germany as the aftermath of war. The question arises whether this may be due to the increase of the endemic area owing to the deterioration of hygiene or whether it was due to importation of fresh cases. The incidence of malaria in Germany in the period 1945–1947 is important for the present purpose. No less than 13,826 cases of malaria were notified, and of these 3,561 were indigenous. These figures must be regarded as minimal, because in the post-war period public notification became disorganized and this had a distinct influence on hygiene. By far the greatest number of autochthonous cases were observed in 1946 (2,335), while the decline in 1947 (1,226) should be regarded not so much as the beginning of a definite diminution, but as a result of unfavourable meteorological conditions for breeding the transmitting species of *Anopheles*. The most heavily infected areas were the towns of Frankfurt on Oder and Berlin, also the districts of

Lebus and Bernau and the whole of Schleswig-Holstein—in these an increase of endemiological distribution has taken place. A very important epidemiological consideration in this epicrisis has been the existence of a reservoir of infection and the opportunities which have been afforded for its spread by the fluctuations and herding together of the population. But, apart from this, it is an entomological problem and depends upon the prevalence of *Anopheles* and especially upon the presence of appropriate races of *A. maculipennis*. Especially important is the influence of microclimate upon the distribution and predilection of *Anopheles* and their intimate human relationships.

In addition to the monthly increase of fresh infections the problem of periodic recurrences of clinical manifestations comes into play. The Dutch view that the northern European type of *Plasmodium vivax* recurs at yearly intervals and that, generally speaking, the incubation period may be prolonged to such an interval could not be confirmed in Germany. *P. Manson-Bahr*

SWAROOP, S. **Forecasting of Epidemic Malaria in the Punjab, India.** *Amer. J. Trop. Med.* 1949, Jan., v. 29, No. 1, 1–17, 4 charts.

In 1921 the Punjab Government undertook the task of preparing annual forecasts of the probable extent of epidemic malaria, and after some preliminary work the forecasts assumed a standard form in 1923. They were at first prepared by GILL who himself devised the method based primarily on observations made by CHRISTOPHERS, but were later prepared by YACOB [see YACOB & SWAROOP, this *Bulletin*, 1945, v. 42, 620]. They were based on a consideration of the rainfall, the spleen rate, the epidemic potential or co-efficient of variation of " fever " mortality during the month of October since 1868, and the economic conditions represented by food prices.

On the partition of the Punjab, and hence the ending of these forecasts in their standard form, the author submits their results since 1923 to statistical analysis. He shows that they attained a high degree of general accuracy which has not varied materially in different periods or between the times when Gill and Yacob were responsible. There has been a steady decline in the trend of the annual epidemic figures from 1867 onwards, and epidemics appear to run in a cycle of eight years, though the author accepts this observation with caution. On statistical analysis of the utility of the factors on which forecasts are based, the author shows a previously unsuspected correlation between epidemic happenings and rainfall in the previous May (co-efficient of correlation 0·563) which should make earlier forecasts possible in future, and finds that contrary to Gill's opinions the spleen rate is not significant in forecasting so that its estimation may be omitted without loss of accuracy. [This is an excellent statistical analysis of a pioneer service. Though partition may alter the form of forecasts it would be very regrettable if they should be discontinued.] *G. Macdonald*

MATTINGLY, P. F. **Anopheline Pupae (Diptera, Culicidae) from West Africa.** *Ann. Trop. Med. & Parasit.* 1949, Apr., v. 43, No. 1, 23–5, 2 figs.

This paper contains descriptions of the pupae of *Anopheles rufipes* var. *ingrami* and *A. flavicosta* and indicates the position of the latter species in the identification key given by DE MEILLON [this *Bulletin*, 1948, v. 45, 295]. *H. S. Leeson*

VAN DER KUYP, E. **Preliminary Report on the Subgenus** *Nyssorhynchus* **(***Diptera, Culicidae***) of Surinam (Dutch Guiana).** *Documenta Neerlandica et Indonesica de Morbis Tropicis.* Amsterdam. 1949, Mar., v. 1, No. 1, 67–8.

" In June, 1946, the following Anophelines of the subgenus *Nyssorhynchus* were collected by the author in Surinam : *A. darlingi darlingi* Root, *A. darlingi paulistensis* Galvão, Lane & Correia (this may not be a valid species), *A. aquasalis* Curry, *A. oswaldoi* Peryassú, *A. triannulatus davisi* Paterson & Shannon and *A. nuñez-tovari* Gabaldon."

BATES, M. & DE ZULUETA, J. **The Seasonal Cycle of Anopheline Mosquitoes in a Pond in Eastern Colombia.** *Amer. J. Trop. Med.* 1949, Jan., v. 29, No. 1, 129–50, 11 figs. [27 refs.]

For some years the authors have studied the seasonal cycle of anopheline mosquitoes in the neighbourhood of Villavicencio in Colombia. Though the observations on larvae recorded in this paper cover one year only and concern anophelines breeding in two small contiguous ponds, they, nevertheless, accord completely with the previous year's observations and with those more general observations made over some seven years.

The most common species breeding in these ponds are *Anopheles rangeli, A. strodei* and *A. triannulatus* ; larvae of *A. darlingi, A. albitarsis, A. argyritarsis* and *A. pseudopunctipennis* also occur. The climate is uniformly equatorial and conditions in the aquatic habitat are stable. There is, however, a seasonal succession of species and a fluctuation in abundance of these anophelines ; *A. rangeli* reaches its peak in June, *A. strodei* and *A. triannulatus* have their peaks in January. Peaks in larval population (all instars) either coincide with or slightly precede adult peaks (all species) and the relative abundance of 1st and 4th stage larvae correspond closely for each of the common species. Fluctuations in the percentage of larvae reaching the 4th instar are not great and mortality is always highest when larvae are most numerous. The seasonal fluctuations in the anopheline populations cannot be accounted for by any change in the water temperature because it is so remarkably constant ; or by seasonal changes in the organic content of the water, for this never touches critical limits. The authors have the impression that the factors affecting population fluctuations operate in the adult rather than in the larval stage, and conclude that more attention needs to be paid to the environments to which the adult anophelines are exposed. *H. S. Leeson*

OKABAYASHI, A. **Some Pathologic Aspects of Malaria Infection and Malaria under Conditions of Malnutrition.** *Japanese Med. J.* 1948, Aug., v. 1, No. 4, 295–302, 14 figs.

This is a confused and erratic account of the author's views concerning the pathogenesis of the morphological and physiological changes developing in tissue in malaria. He regards malaria as a " special type of septicaemia with all the characteristics of a disseminating general infection ". He refers briefly to general and localized tissue reactions and the pathogenesis of certain " symptoms " including anaemia and jaundice. He regards the latter as haematogenous in nature, and resulting from haemolysis of erythrocytes. Blackwater fever is explained on the grounds of allergy. The paper is poorly printed and written in a sort of scientific jargon which often makes it difficult to understand. As an example of this, I quote the following : " The malnutrition precipitated by an attack of malaria is morphologically distinguished by the persistence of the malarial angiomesenchymal tissue reaction."

A claim is made that during studies of human malaria bodies were found in endothelial cells of the brain capillaries which suggested exo-erythrocytic forms of the parasite. [Species not disclosed.] A series of drawings of these bodies is included. This is perhaps the only excuse for reviewing the paper.

B. G. Maegraith

Benitez Calvo, L. A. Algunas consideraciones y tecnicas en el serodiagnostico del paludismo. [**Observations on Serodiagnostic Methods in Malaria.**] *Med. Colonial.* Madrid. 1949, May 1, v. 13, No. 5, 383–98. [22 refs.]

A general review.

Peel, E. & van Hoof, L. Le paludisme à la maternité indigène de Léopoldville. [**Malaria in African Parturient Mothers in Léopoldville.**] *Ann. Soc. Belge de Méd. Trop.* 1948, Dec. 31, v. 28, No. 4, 413–20.

This paper gives the results of many years' work in the Congo on the subject of malaria in pregnancy. The routine adopted was to take blood slides from all women admitted to the maternity annexe at Léopoldville and to repeat this after parturition, when the blood of the placenta and of the newborn child was also examined. If the placental blood showed malaria parasites, the child's blood was re-examined a number of times. If the child died, a post-mortem examination was usually made.

Malaria is hyperendemic in Léopoldville, all the young children appear to be infected and there is no doubt that the women seen in this investigation were all infected with malaria. Even after treatment with quinine in the later stages of pregnancy, the women showed a parasite rate as high as 65 per cent. As the authors truly state, it is only a question of perseverance to find parasites in every case.

Four hundred and three mothers were investigated: parasites were not found in 136; 198 showed parasites in the placenta. *P. falciparum* was the dominant species; there were 24 examples of *P. malariae* and 8 of *P. vivax* or *P. ovale* in the maternal blood. It was difficult to differentiate the last two species from each other owing to the scarcity of parasites. Malaria could sometimes be diagnosed in the absence of parasites by the presence of malarial pigment in the phagocytes. The distribution of species in the placental blood was much the same as in the peripheral blood, with an even greater dominance of *P. falciparum* (99 per cent. of all infections instead of 87 per cent.). The appearance of this parasite in the placenta contrasted strongly with the blood forms, mature parasites often being found in large numbers in the former, sometimes with a very large number of merozoites grouped regularly around a single block of pigment. The average number of merozoites in a schizont in the placenta was 30, in the blood, 20. The authors think that these larger merozoites of the blood may possess a capacity for further division, as illustrated by the presence of rings with two dots of chromatin. Maurer's clefts persisted in infected erythrocytes until the chromatin began to divide. Gametocytes were very rare.

The nature of the phagocytes (including their origin from lymphocytes of the blood [see also this *Bulletin*, 1939, v. 36, 492] in the intervillous spaces of the placenta is discussed and their tremendous capacity for concentration and for storage of pigment. In cases where the infection was severe and chronic, the most massive infiltration of the organ occurred.

Three hundred and ninety-three of the newly born children were examined: 27 died within 10 days of birth and 14 of these were examined *post-mortem*. The examination comprised a long and minute search for parasites in the blood, but in not a single case was a malaria parasite found. In other words,

in this long series made up of a great variety of infections, congenital malaria was absent. It is suggested that possibly the extraordinary number of phagocytes in the placenta constitutes an obstacle to the trans-placental passage of the parasite. Malaria in the mother appeared to affect the health of the infant by causing a low weight (2,000–2,500 gm.) at birth. Deaths in the newly born were 6·8 per cent. during the first eight days, but syphilis and other conditions were found to be the cause as well as malaria.

P. C. C. Garnham

Binaghi, G. Un caso di malaria atipica. (Utilità diagnostica della splenopuntura.) [**A Case of Atypical Malaria diagnosed by Splenic Puncture.**] Reprinted from *Rass. Med. Sarda.* 1947, Suppl. to No. 3/4, 7 pp. in *Lavori dell'Istituto d'Igiene d. Univ. di Cagliari* ***1940–1946.*** 1949.

The following is a translation of the author's summary :—

The author describes a case of clinically atypical malaria in which the diagnosis was made after a long delay by the finding of parasites on the fourth splenic puncture, while several examinations of the peripheral blood and sternal puncture were persistently negative. *H. J. O'D. Burke-Gaffney*

i. Mackerras, M. J. & Ercole, Q. N. **Some Observations on the Action of Quinine, Atebrin, and Plasmoquine on** *Plasmodium vivax. Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 443–54, 3 graphs & 4 coloured figs. on 4 pls. [16 refs.]

ii. —— & ——. **Observations on the Action of Quinine, Atebrin and Plasmoquine on the Gametocytes of** *Plasmodium falciparum. Ibid.* 455–63, 2 graphs.

i. Many theories have been put forward to explain the mode of action of quinine and other drugs on malarial parasites. The *in vitro* studies by Christophers and Fulton [this *Bulletin*, 1938, v. 35, 709] and of American authors subsequently, up to the investigation of Moulder (*ibid.*, 1949, v. 46, 445), have shown that the action is probably direct on the parasites. The present authors have recently described [this *Bulletin*, 1948, v. 45, 305] the changes which occur in the sexual and asexual forms of human malaria during normal development in the peripheral blood and after treatment with paludrine. The present experiments, carried out with Melanesian strains of *P. vivax* transmitted by *Anopheles punctulatus punctulatus* to susceptible white hosts, were made while the authors formed part of the Medical Research Unit at Cairns, Australia. The effect of quinine, atebrin (mepacrine) and plasmoquine (pamaquin) on the growth and development of the parasites in the patients' blood was observed by means of fresh preparations and stained films, and in mosquitoes which were fed on the infected hosts during treatment. The appearance of parasites developing normally and those in contact with the drugs are shown in coloured plates. It appeared that quinine and atebrin acted similarly, the latter more effectively, on the erythrocytic stages of the parasite which metabolize haemoglobin, as evidenced by pigment production. Growth was affected and morphological changes were apparent after a few hours. Mature gametocytes were not affected, and developed normally in the mosquito. Plasmoquine had some effect on all stages of asexual growth, and to some extent on gametocytes, for no mosquito infections were obtained 42 hours after treatment started.

ii. In continuation of the experiments described above, the effect of the same three drugs on the gametocytes of *P. falciparum* was studied. It was confirmed that therapeutic doses of quinine or atebrin, did not influence the numbers, morphology (except that atebrin sometimes gave rise to unpigmented

forms, as noted previously by SINTON [this *Bulletin*, 1939, v. 36, 396]) or infectivity of mature forms to mosquitoes. Quinine did, however, appear to affect young forms adversely, and numbers were ultimately reduced. This effect of quinine is comparable to that noted by BLACK [this *Bulletin*, 1947, v. 44, 176] in the case of trophozoites *in vitro*. The marked effect of plasmoquine on gametocytes was also confirmed. When mosquitoes were fed on patients three hours after treatment with 10 mgm. of this substance infection still occurred, but its intensity was reduced after six hours, and notably so after nine hours. At the end of 15 hours no gland infections were noted in spite of the presence of numerous sexual forms in the patient's blood up to 25 hours after treatment, when exflagellation still occurred. Thereafter the gametocytes gradually degenerated and disappeared. *J. D. Fulton*

WAR OFFICE. **Malaria Relapses treated with Quinine and Quinine Substitutes.** *Statistical Report on the Health of the Army 1943–1945*. 1948, 273–6, 1 chart.

In accordance with a directive sent to military hospitals in the United Kingdom all cases of malaria relapse were to be treated with one or other of the two following courses of treatment, without any further antimalarial maintenance treatment :

Course I. Mepacrine 0·2 gm., with a copious draught of fluid, every six hours for 48 hours, then 0·1 gm. thrice daily after food for 10 days.

Course II. Quinine in solution ten grains and pamaquin 10 mgm., concurrently, thrice daily after food for 10 days. Patients to remain in hospital throughout treatment ; pamaquin to be discontinued if cyanosis or abdominal colic appear.

Six hundred and fifty patients with *P. vivax* relapses were treated with Course I ; 584 with Course II. During a period of five months from the end of treatment the percentage of patients who relapsed after Course I was 34 ; after Course II, 10·3. Relapses after Course II occurred earlier (maximum in fifth week) than after Course I (maximum in eighth week).

The same superiority of Course II in preventing relapse was noted in the treatment of first attacks. The relapse rate after the treatment of 100 such cases with Course I was 29 per cent. ; of 76 cases with Course II, 5 per cent. (five months period).

A graph which is appended to the text illustrates the periodicity of *P. vivax* relapses with a major peak in the second and a minor peak in the ninth month. *Norman White*

WAR OFFICE. **B. T. Malaria Relapses treated with Paludrine.** *Statistical Report on the Health of the Army 1943–1945*. 1948, 277.

Male patients suffering from relapsing *P. vivax* malaria admitted to the Colchester Military Hospital were treated alternately with one of the three following methods of treatment :—

A. Quinine 10 grains and pamaquin 10 mgm. thrice daily for 10 days.
B. Paludrine [proguanil] 25 mgm. twice daily for 10 days.
C. Paludrine 250 mgm. twice daily for 10 days.

Every third patient received one and the same treatment ; consecutive patients in order of reception received different treatments. Follow-up was by written questionary. Six months after the end of treatment the results were :—

Course A. 107 treated ; 19·6 per cent. had relapsed.
Course B. 108 treated ; 54·4 per cent. had relapsed.
Course C. 107 treated ; 48·6 per cent. had relapsed.

The paludrine courses were much less effective in preventing relapse than quinine-pamaquin, but it may be that more frequent administration of paludrine would give results as good as, or better than, those obtained with quinine-pamaquin. *Norman White*

COATNEY, G. R. **Chemotherapy of Malaria.** *Bol. Oficina Sanitaria Panamericana.* 1949, Jan., v. 28, No. 1, 27–37, 4 figs. [42 refs.]

This is a succinct account of the newer antimalarials which should prove of value to those called upon to treat the various forms of the infection. Much of the co-ordinated search for new drugs of this type was carried out in the United States and to a lesser extent in Britain. In the U.S.A. more than 14,000 compounds were tested against avian malarial infections and the pharmacology and toxicology of a proportion were studied in mammals. About 100 were tested in human patients. In view of the shortcomings of quinine, SHANNON and co-workers made an intensive physiological and antimalarial study of atebrin [mepacrine] and, in conjunction with the work of FAIRLEY, the knowledge thus acquired allowed this substance to be used with remarkable success as a suppressant in the field. Chloroquine (SN 7618) a 4-aminoquinoline, synthesized and tested by the Germans, to a limited extent, under the name resochin as early as 1934, ranks high as a therapeutic and suppressive agent. [For a description of its properties see this *Bulletin*, 1946, v. 43, 708. KIKUTH has recently stated that this substance was captured in North Africa in 1942 and taken to America where its constitution was discovered. The present account of its history differs somewhat.] It may be given intramuscularly to comatose patients and rapidly relieves acute attacks of the three human malarias. Other substances of value in the series are sontochin (SN 6911) (a 3-methylderivative of resochin, also made by the Germans), oxychloroquine (SN 8317) and camoquin (SN 10,751) Paludrine, the chief British contribution to this field of research, is of outstanding value as a therapeutic and suppressive agent, with a wide margin of safety. In practice the author does not consider it superior to chloroquine. Pentaquine (SN 13,276) [this *Bulletin*, 1947, v. 44, 396] and isopentaquine (SN 13,274) which are 8-aminoquinolines related to pamaquin [plasmoquine] appear to have definite advantages over the latter. When given along with quinine the relapse rate in benign tertian malaria was considerably lowered. Although less toxic than pamaquin these two substances require to be given under medical supervision because of danger to the circulatory system and their routine use with quinine is not recommended.

[Abstracts of papers on the chemotherapy of these substances have appeared in this *Bulletin*.] *J. D. Fulton*

KIKUTH, W. & MUDROW-REICHENOW, Lilly. Neue Wege in der Chemotherapie der Malaria. [**New Developments in the Chemotherapy of Malaria.**] *Deut. med. Woch.* 1949, Jan. 28, v. 74, No. 4, 97–101. [29 refs.]

This is a short review of progress in the chemotherapy of malaria dating from the discovery of plasmoquine and atebrin [mepacrine] to the present day. It has a "hard luck" ring about it. During the war when it was found that quinine in reasonable doses failed to act satisfactorily as prophylactic or suppressant, atebrin in daily doses of 0·1 gm. was found to be effective as suppressant. Before the war a certain amount of doubt was expressed about the value of atebrin in Britain, and in Germany search was therefore made for a drug to replace it. Resochin and sontochin were synthesized there before

the late war. They bear a constitutional resemblance to atebrin, if one benzene ring and substituents be removed from the latter, resochin being 4-diethylaminoisopentylamino-7-chloroquinoline and sontochin its 3-methyl derivative. Both resembled atebrin in properties, and were active against schizonts but had no causal prophylactic action. They did not colour the skin and could be used with plasmoquine [pamaquin] without giving rise to untoward effects. In 1943 sontochin was captured by the Allies in North Africa. The whole series including resochin was discovered as a result of intensive work in America [see also COATNEY, above]. The latter was named chloroquine (SN 7618), and its properties have been fully described [this *Bulletin*, 1946, v. 43, 708]. Resochin and sontochin were also tested by FAIRLEY at Cairns, Australia, during the late war. Nivaquine C is the dihydrochloride of sontochin, other salts were given the names Nivaquine M or R, and were preferred by the French to atebrin. Reference is also made to the discovery of paludrine, some space being devoted to the fact that resistance to it has been induced in *P. gallinaceum* but no reference is made to the fact that similar resistance to plasmoquine was readily induced in *P. knowlesi*. The search for something to replace plasmoquine, which was toxic, led to the discovery of Certuna in Germany before the war and to pentaquine in the U.S.A. during the war, but neither has come into general use. Although large numbers of new sulphonamides have been synthesized, all have proved disappointing in treatment of malaria. Endochin, a 4-hydroxy-quinaldine tested by the author had marked prophylactic properties in bird malaria but was inactive in human and monkey malaria. In a search for guidance in the synthesis of active substances in malaria later work has tried to elucidate the metabolic requirements of plasmodia and the mechanism of drug action. It remains to be seen whether the more scientific approach will yield more fruitful results than the older method of trial and error.

[All the investigations mentioned in this article have been abstracted in this *Bulletin*.] *J. D. Fulton*

COVELL, G., NICOL, W. D., SHUTE, P. G. & MARYON, M. **Studies on a West African Strain of *Plasmodium falciparum*. II. The Efficacy of Paludrine (Proguanil) as a Therapeutic Agent.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 465–76, 1 chart. [10 refs.]

The authors describe therapeutic trials with paludrine, carried out at Horton, with a W. African strain of *P. falciparum* whose origin was described in Pt. 1 of this series [this *Bulletin*, 1949, v. 46, 437]. The object was to clarify some outstanding questions with regard to treatment of infections with this strain. During maintenance of the strain by serial blood and mosquito transmission (*A. stephensi* from India were used), it was only in contact with paludrine on one occasion. All the patients were neurosyphilitics who had undergone malarial therapy 9 or more years earlier. Successful trials of this drug with W. African and New Guinea strains of *P. falciparum* have previously been reported [this *Bulletin*, 1946, v. 43, 402, 527 ; 1947, v. 44, 282]. In Malaya and India results were not so satisfactory. In Sardinia, BETTINI [this *Bulletin*, 1948, v. 45, 861] found that the clinical response in malignant tertian infections was satisfactory, but relapses occurred. At Horton 31 patients were inoculated intravenously with sporozoites from two infected mosquitoes of the same batch. It appeared that the numbers of sporozoites injected did not appreciably affect the severity of the attack or the number of relapses. The patients were divided into 6 groups and, when temperatures reached 100°F. and parasites were present in the peripheral blood, treatment was given as shown :—

Group	Number in each group	System of Treatment	Result
1	5	Paludrine mgm. 300 once daily for 14 days	All relapsed within 3 weeks. One had second relapse after further treatment.
2	5	Paludrine mgm. 300 twice daily for 7 days	4–5 relapsed within 3 weeks and when re-treated there were 2 further relapses.
3	5	Paludrine mgm. 300 twice daily for 10 days, plus mepacrine mgm. 300 thrice daily on the first day only.	No relapse over 6 months.
4	5	Paludrine mgm. 300 twice daily for 10 days, plus quinine hydrochloride grains 10 thrice daily on the first day only	No relapse over 6 months.
5	5	Quinine hydrochloride grains 10 twice daily for 10 days	No relapse over 6 months.
6	2	Quinine hydrochloride grains 10 thrice daily one day only	The rapidity of clinical response was in the order mepacrine, paludrine, quinine. For clinical reasons the treatment outlined was not adhered to.
	2	Mepacrine mgm. 300 thrice on one day only	
	2	Paludrine mgm. 300 thrice on one day only	

Gametocytes disappeared from the blood of all patients except one treated with paludrine and quinine. In those who had relapses gametocytes were present except in one case. Paludrine was effective in controlling the clinical attack as other authors have found, but asexual parasites disappeared from the peripheral blood more slowly than after treatment with mepacrine or quinine. Unlike FAIRLEY, who used a New Guinea strain of the parasite, and obtained a radical cure in 46 out of 47 cases, the present authors were unable to effect radical cure with the Lagos strain. The series is small, and it is possible that the relapses are associated with early treatment of the primary attack in absence of immunity. Because of the favourable results obtained by reinforcing paludrine treatment with mepacrine, such a course is recommended in all cases of this potentially dangerous infection. The replacement of mepacrine by quinine is not recommended, although both drugs helped to prevent relapses. As found by other authors paludrine prevented development of gametocytes in mosquitoes. The following paragraph is taken from the authors' summary :—

" It is considered that a course of paludrine mg. 300 twice daily for 10 days, reinforced with mepacrine mg. 900 given in three doses on the first day of

treatment and followed by a maintenance dose of paludrine mg. 100 daily for the ensuing 6 weeks would fulfil the main objectives in the treatment of falciparum malaria, namely, rapid termination of the clinical attack, a high radical cure rate, sterilization of gametocytes and minimum risk of injurious side effects." *J. D. Fulton*

Abbott, P. H. **Proguanil in the Sudan.** [Correspondence.] *Brit. Med. J.* 1949, Mar. 5, 413–14.

The writer of this letter states that he has found proguanil (paludrine) to be a very valuable malaria prophylactic in his district of the Southern Sudan where *P. falciparum* malaria is hyperendemic. For the last two years it has afforded very adequate protection to a number of British officials and Northern Sudanese Arabs who have been under his care. If 350 mgm. per week be taken regularly (half a tablet each morning at breakfast time) the chances of developing a clinical attack of malaria are very small indeed. In the treatment of *P. falciparum* malaria proguanil has, however, given disappointing results. Doses of 100 mgm. thrice daily for ten days reduce the fever less rapidly than does either quinine or mepacrine : positive blood films have been found on the fifth day of such a régime. *Norman White*

Ferro-Luzzi, G. Nuovi esperimenti sul trattamento paludrinico della terzana maligna in Eritrea. [**Further Experiments on the Treatment of *P. falciparum* Malaria with Paludrine in Eritrea.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1948, v. 8, Nos. 5/6, 209–14. English summary.

The author has previously reported the failure of paludrine in doses of 0·2 to 0·3 gm. a day for ten days in the treatment of patients suffering from *P. falciparum* malaria in Eritrea [this *Bulletin*, 1949, v. 46, 213]. In this paper he records the results of the treatment of 50 additional patients with 0·6 gm. paludrine a day for ten days, and 50 patients with mepacrine for seven days and pamaquin for a further five days. There was little if anything to choose between the two methods of treatment with regard to the duration of fever or the persistence of trophozoites in the blood. With regard to the relapse rate, however, paludrine showed up badly. Within 20 days from the end of treatment with paludrine 34 per cent. of the patients relapsed, as compared with 2 per cent. after mepacrine-pamaquin treatment. It is suggested that the local Eritrean strains of *P. falciparum* have a particular resistance against paludrine. *Norman White*

Canet, J. Efficacité comparée de la nivaquine et de la paludrine dans le traitement curatif de l'accès palustre aigu, en Indochine. [**Comparative Efficacy of Nivaquine and Paludrine in the Treatment of Acute Malaria in Indo-China.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 11/12, 661–6.

In a hospital in Indo-China, 140 patients suffering from acute attacks of malaria were treated with nivaquine, and 140 with paludrine. The dose of each drug was 0·30 gm. a day. The two groups of patients were comparable : in each there were 120 *P. falciparum* and 20 *P. vivax* infections. Both drugs were effective, but the action of nivaquine was more rapid than that of paludrine both as regards the control of fever and the rate of disappearance of schizonts from the peripheral blood. On the morning of the third day 93 per cent. of the *P. falciparum* patients treated with nivaquine were afebrile as compared with 66 per cent. of the paludrine-treated patients. On the fourth evening 76 per cent. of the nivaquine *P. falciparum* patients were free from demonstrable parasites as compared with 60 per cent. of the paludrine group. Similarly with

the *P. vivax* infections: on the third evening 95 per cent. of the nivaquine patients were afebrile as compared with 70 per cent. of the paludrine patients: on the sixth day 45 per cent. of patients receiving paludrine harboured parasites as compared with 5 per cent. of the nivaquine treated patients.

Neither drug had any action against the sexual forms of *P. falciparum*, and nivaquine none against sexual forms of *P. vivax*. The possible activity of paludrine against *P. vivax* gametocytes calls for further inquiry.

The curative action of nivaquine on the general symptoms of acute malaria was more prompt and more constant than was that of paludrine.

Both drugs were equally well supported; symptoms of intolerance were rare and insignificant. The author considers both drugs to be a distinct advance on older synthetic remedies such as mepacrine. *Norman White*

Coggeshall, L. T. & Rice, F. A. **Cure of Chronic Vivax Malaria with Pentaquine.** *J. Amer. Med. Ass.* 1949, Feb. 12, v. 139, No. 7, 437–8.

This paper reports the treatment of 185 ex-servicemen, suffering from relapsing *P. vivax* malaria, with pentaquine and quinine. Pentaquine is a derivative of pamaquin than which it is less toxic and more effective. Infection in 154 of these men had been acquired in the South-west Pacific. The majority had been suffering from relapses every four to six weeks before treatment began. Pentaquine 30 mgm. and quinine 2 gm. were given daily for 14 days: later the dose of quinine was reduced to 1·0 gm. daily. The reduced doses of quinine were given in 67 cases and proved to be as effective as the larger doses. After treatment the patients were observed for six months or longer. In only ten was a further relapse noted, with parasites in the blood. Ten others had chills, but no parasites could be found in their blood smears. One hundred and sixty-three have had no further symptoms referable to malaria. A striking relief from the subjective symptoms associated with chronic malaria was experienced by nearly all. The treatment was ambulatory and did not necessitate interruption of normal activities. Toxic reactions were largely those associated with the use of quinine. *Norman White*

Berg, S. S. & Newbery, G. **The Search for Chemotherapeutic Amidines. Part X. Substituted 4 : 4′-Diamidino-$\alpha\omega$-Diphenoxyalkanes and -Diphenyl Ethers.** *J. Chem. Soc.* 1949, Mar., 642–8.

Cymerman, J. & Short, W. F. **Amidines. Part XII. Preparation of 9-Substituted Phenanthridines from N-2-Diphenylyl-amidines.** *J. Chem. Soc.* 1949, Mar., 703–7.

Kirby, K. S. **Quinamine. Part III. *iso*Quinamine.** *J. Chem. Soc.* 1949, Mar., 735–7.

McCoubrey, A. & Mathieson, D. W. **Contributions to the Chemistry of *iso*Quinolines. Part I. The Synthesis of Diamino-1-Phenyl*iso*quinoline Methiodides in a Search for New Trypanocides, with some Observations on the Nitration of 1-Phenyl*iso*quinoline.** *J. Chem. Soc.* 1949, Mar., 696–701, 2 charts.

Davey, F. & Smith, M. **Malaria Prophylaxis with Proguanil.** [Correspondence.] *Brit. Med. J.* 1949, May 28, 956.

The writers of this letter refer to reports of *falciparum* malaria occurring in persons taking more than 0·1 gm. of proguanil on alternate days [this *Bulletin*, 1948, v. 45, 972; *Brit. Med. J.*, 1949, Feb. 19, 324], and to the recommendations

of these authors, implemented by the Colonial Medical Research Committee [this *Bulletin*, 1949, v. 46, 608], that the prophylactic dose of proguanil should be 0·1 gm. daily.

They then describe a case in an endemic area in Nigeria where malaria due to *P. falciparum* occurred in a European nursing sister who had been taking 0·1 gm. of proguanil daily as a prophylactic.

The patient had been in Nigeria for nine months, and during the whole of that time had only occasionally missed taking a regular daily tablet of proguanil —at most this omission amounted to one a week and usually much less than this. She had had several mild and short attacks of pyrexia and in the absence of proved parasitaemia and because of their clinical nature the attacks were considered to be caused by a dengue-like fever. After the last attack she increased her dose of proguanil to 0·2 gm. daily for eight days and then reverted to 0·1 gm. daily.

A month later, she developed an evening temperature of 101°F. : thick blood films then revealed the presence of 2 to 20 young *P. falciparum* trophozoites per microscopic field. Thin films showed some red cells with two or three parasites, some parasites with double chromatin dots and the presence of accolé forms, a picture typical of the acute *falciparum* infection seen locally in children.

Increased proguanil and mepacrine aborted the attack and the temperature fell and remained normal from the next day. On the 14th day of the attack, gametocytes were found in the blood.

It seems clear that in this case a daily dose of 0·1 gm. of proguanil was insufficient to prevent a break-through of *falciparum* malaria.

H. J. O'D. Burke-Gaffney

Berberian, D. A. & Dennis, E. W. **Field Experiments with Chloroquine Diphosphate.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 755–76, 1 chart.

The observations recorded were designed to test the value of chloroquine diphosphate in the treatment and prevention of malaria in rural communities. For this purpose two villages in Lebanon, Saideh and Azouniyeh, were selected. Malaria is hyperendemic in both, the transmission season lasting from the end of April to the end of November. *A. sacharovi* is the chief vector in Saideh ; in Azouniyeh *A. superpictus* is predominant, but *A. claviger* and *A. marteri* also occur. The populations of the villages number about 215 and 200 respectively.

In Saideh 93 persons were examined on August 25, 1946. These included all who were acutely ill on that day, those who had been ill recently and those who agreed to take suppressive treatment. Twenty-six of these persons were febrile and were each given a therapeutic course of chloroquine diphosphate. The remainder each received a single suppressive dose of the drug. This procedure was repeated at weekly intervals. On each occasion the numerous cases of fever that occurred among the " control " group of the population were treated and other members of the control group demanded and received suppressive medication. By November 18 all the villagers were receiving weekly suppressive doses of chloroquine diphosphate : this was continued till April 7, 1947. During the period of observation 70 attacks of malaria occurred among the diminishing control group ; there were no attacks among those on suppressive medication.

The therapeutic dosage was : for children under five years a total dose of 2½ tablets (0·25 gm. each) spread over three days ; for children 5 to 10 a total dose of 2½ to 5 tablets ; for older ages a total of 5 tablets. This adult dose was insufficient in 7 of 45 cases, 3 *P. vivax* and 4 *P. falciparum* infections. In these cases a second course was given comprising double the dose prescribed for the

first treatment. The adult suppressive dose was 0·5 gm. 2 tablets, in a single dose once a week.

When chloroquine suppression ceased on April 7 an intensive treatment of the village with DDT started. The DDT treatment was repeated in July. During the period April 8 to November 23, 1947 only three cases of malaria occurred in Saideh, two in May and one in June. Two of these were recurrences and one probably a fresh infection.

Observations in Azouniyeh were on somewhat different lines but they support the conclusion that chloroquine diphosphate is a most effective curative and suppressive drug for malaria as it occurs in the Middle East; it is effective against *P. vivax*, *P. falciparum* and *P. malariae*. Effective doses may be given to infants and during the course of pregnancy. By combining weekly prophylactic medication with DDT measures it is possible to eradicate malaria from a community within the period of a single transmission season.

Norman White

STIERLI, H. & STENBURG, R. L. **Some Developments in Insecticide Dispersal Equipment.** *J. National Malaria Soc.* 1949, Mar., v. 8, No. 1, 100–108, 7 figs.

There is a need for the improvement of equipment for spraying insecticides and the author considers several defects in common equipment and the means of remedying them. The hand-pump sprayers of the knapsack type are very wasteful of operators' time, and some form of mechanical air compressor to charge tanks as car tyres are commonly charged is considered essential in any efficient scheme. Aluminium is better than other metals for the manufacture of tanks, and there is need for improvement in hosing, shut-off valves and other parts.

Several types of sprayer made from surplus war materials, such as aircraft compressed-air tanks, are described, together with a new design made from fresh material. In essence it consists of two cylindrical aluminium tanks of 5½ in. and 8 in. diameter, the smaller holding 2 gallons of fluid is situated within the larger, the space between acting as the air reservoir. It is given an initial charge of 80 lb. per sq. inch and will discharge the liquid contents at a constant pressure of 40 lb. per sq. inch. A modification of a previous shut-off valve which has quick action and prevents leakage round the release pin is described. Brief information is given about an "Institution Sprayer" with an electric or petrol power unit suitable for the routine treatment of hospital wards, warehouses and large buildings, and of a "Multi-Purpose Insecticide-Dispersing Machine" which consists of a collection of apparatus on a truck capable of undertaking a wide range of insecticide work including the distribution of dust and liquid. [The modifications proposed seem sound and the apparatus described is probably a considerable advance. In the absence of scale drawings it is only possible to understand and not to re-duplicate the designs.]

G. Macdonald

FERGUSON, F. F., UPHOLT, W. M. & SIMMONS, S. W. **A Summary of the Experimental Use of DDT as a Mosquito Larvicide.** *J. National Malaria Soc.* 1949, Mar., v. 8, No. 1, 32–49. [140 refs.]

This is itself a highly condensed summary. It consists of a classified account of the literature on the use of DDT as a mosquito larvicide with a very full bibliography, with some authoritative opinions on present trends in practice. It should be consulted in the original by all interested in the subject.

The account covers all aspects of the subject and a few outstanding points may usefully be listed. United States authorities recommend that the dosage should not exceed 0·1 lb. DDT per acre. Where reasonable precautions are taken DDT larvicides may be used without danger to the health of workers. Though larvae are extremely susceptible to DDT, pupae are very resistant. Residual larvicide action has not been achieved except under exceptional conditions, the explanation propounded being that DDT is absorbed upon the organic soil components of a pond-bottom complex. There is no significant difference between the susceptibility of different types of larvae. Pond wild life may readily be destroyed by DDT, particularly by emulsions, unless great care is used. Of the many methods of application used the author considers that the oil/mist technique described by Ferguson *et al.* [this *Bulletin*, 1947, v. 44, 645] is possibly the most effective manual method. Several references are given to air distribution and to the effect of particle size and its measurement.

The author considers that future development in the field of DDT liquid larviciding may be chiefly centred in basic studies of the type of solvent and solvent spraying agent, and continued efforts to improve dispersion equipment.

G. Macdonald

Nair, C. P. **Effect of D.D.T. Barrier Spray in *A. sundaicus* Area in Malaya.** *Med. J. Malaya.* 1949, Mar., v. 3, No. 3, 198–203, 1 map.

DDT as a 5 per cent. solution in kerosene was applied as a barrier spray to a strip of ground 50 yards broad around experimental sites. The dose was 6 gallons per acre (1·1 oz. DDT per 1,000 sq. ft.) and the fluid was applied from hand atomizing sprayers on a carefully regulated technique. In one experimental area the barrier spray only was applied. In the second it was supplemented by spraying the external walls of the houses up to a height of 7 ft. In the third it was supplemented by this same external spray and an internal house spray delivered from atomizing guns in the manner common with the use of immediate insecticides. Comparable groups of houses were left as untreated controls.

Mosquito catches showed an immediate disappearance of anophelines (presumably mostly *A. sundaicus*), and a marked reduction in culicines. Observation was stopped when the anophelines in the treated houses reached one-tenth of the number in the untreated, and this occurred between 9 and 14 days, there being no difference in the three areas. *G. Macdonald*

Schmidt, L. H., Genther, Clara S., Fradkin, Rochelle & Squires, Wanda. **Development of Resistance to Chlorguanide (*Paludrine*) during Treatment of Infections with *Plasmodium cynomolgi*.** *J. Pharm. & Exper. Therap.* 1949, Mar., v. 95, No. 3, 382–98, 4 figs. [14 refs.]

While studying the effects of chlorguanide [paludrine] on blood-induced infections of *P. cynomolgi* in rhesus monkeys it was noted that hosts which had earlier been treated with small amounts of the drug were no longer freed from infection by doses normally curative. The strain showed stable characters to other antimalarials. In the experiments now described, infection was also produced by intravenous inoculation of sporozoites from *A. quadrimaculatus*. Drugs were given in aqueous solution by stomach tube twice daily for 7 or 14 days. Blood smears were examined in thick and thin films, and the proportion of the different parasite stages noted. If parasites remained absent from the blood for 8 weeks or more after treatment and failed to reappear within 4 weeks after splenectomy the animal was considered to be cured.

Doses of 0·075 mgm. paludrine or less per kilo were able to suppress parasitaemia, and 0·6 mgm. per kilo effected cure in more than 90 per cent. of cases. It should be noted that in rhesus monkeys this infection is self-limiting within a period of 4 months. Resistance was produced to paludrine by the classical method of serial passage and use of gradually increasing sub-curative doses.

After passage through three monkeys from a host with partially resistant parasites it was found that the maximally tolerated dose of 40 mgm. per kilo of paludrine was non-curative and did not appreciably affect the course of infection, thereby indicating a 2,000-fold resistance. [In this connexion the authors note that only a four-fold resistance to plasmoquine was obtained in *P. knowlesi* infections of rhesus monkeys [this *Bulletin*, 1942, v. 39, 438]. It should be observed, however, that plasmoquine is a toxic drug, and as in their case, the maximum tolerated dose did not influence the infection.] Whereas in the normal strain of *P. cynomolgi* the drug allowed the development of schizonts but prevented segmentation, in the resistant strain growth and reproduction were unaffected, and morphological changes in the parasites were absent. The resistant character persisted unchanged after mosquito passage, and likewise after 6 blood passages over a period of 5 months. The resistance to paludrine did not involve resistance to chloroquine or quinine in blood-induced infections, or to pentaquine in sporozoite-induced infections. No evidence was obtained of induced resistance to quinine, atebrin (quinacrine), chloroquine, oxychloroquine, pamaquin, pentaquine or isopentaquine. The authors believe that these drugs attack the parasite in a different way from paludrine.

A brief discussion is given of the implications of this developed resistance to paludrine. The authors note specially that mature trophozoites and early schizonts of *P. cynomolgi* are affected by the drug without the accompanying morphological changes, which characterize the action of other antimalarials. Also the parasites in contact with paludrine remain for several days in the blood whereas after treatment with other drugs they may disappear in a few hours. They indicate a parallel in the readiness with which resistance of bacteria to the bacteriostatic sulphonamides is produced, as opposed to the difficulty of producing it by bactericidal penicillins. It is possible that the resistance produced in *P. cynomolgi* by paludrine may result from mutation.

[For evidence of acquired resistance in different plasmodia to quinine, plasmoquine, paludrine, see this *Bulletin*, 1921, v. 18, 96 ; 1933, v. 30, 860 ; 1935, v. 32, 116 ; 1942, v. 39, 438 ; 1943, v. 40, 754 ; 1947, v. 44, 969, 970 ; 1948, v. 45, 158.] *J. D. Fulton*

RAGAB, H. A. **Effect of Humidities and Temperatures on the Size and Number of Oocysts of *Plasmodium gallinaceum* transmitted by a Mosquito.** [Correspondence.] *Nature*. 1949, Apr. 23, 643–4.

Aëdes aegypti mosquitoes were infected by allowing them to feed upon chicks whose blood contained numerous gametocytes of *P. gallinaceum*. Batches of twenty of the engorged mosquitoes were then transferred to celluloid cylinders covered with netting and placed in jars of differing humidities, the humidity being controlled by mixtures of sulphuric acid and water, at 50, 60 and 70 per cent. Three of such cylinders were kept at 25°C., three others at 18°C. (A relative humidity of 30 per cent. or of 90 per cent. caused the mosquitoes to die rapidly.) On the sixth day all the mosquitoes remaining alive were dissected and the results were as follows :—

	18°C.			25°C.		
Relative humidity... ...	50	60	70	50	60	70
Number of mosquitoes ...	12	17	15	13	16	14
Mean number of oöcysts ...	11	29	29	11	33	32

The different humidities did not affect the size of the oöcysts (the size was, however, affected to a small degree by the temperature, those kept at 25°C. being about 20 per cent. larger than those at 18°C.), but they clearly had an action on the number of oöcysts, a low humidity reducing the number to nearly a third of the numbers occurring at 60 or 70 per cent. It is stressed that in nature where mosquitoes have access to drinking water, a low humidity in the external environment might not have this effect.

[The optimum conditions for the development of different plasmodia in species of mosquitoes are still imperfectly known; studies such as this are, therefore, valuable.] *P. C. C. Garnham*

GRAY, A. & HILL, J. **Antimalarial Studies in the Quinoline Series.** *Ann. Trop Med. & Parasit.* 1949, Apr., v. 43, No. 1, 32–8. [18 refs.]

The activity of a number of quinoline derivatives has been tested in blood—induced and sporozoite—induced infections of *P. gallinaceum* in which methods already described [this *Bulletin*, 1946, v. 43, 394] were used, and in blood-induced infections of *P. relictum* by the method of Roehl. When pamaquin (plasmoquine), pentaquine and R36 (8-γ-aminopropylamino-6-methoxy quinoline) were converted to the 1 : 2 : 3 : 4-tetrahydro derivatives it was found that they were less active than the unreduced compounds. Toxicity was also reduced in the first two substances by this treatment. The compound R36 was originally shown by TATE & VINCENT [this *Bulletin*, 1934, v. 31, 434] to possess considerable activity in *P. relictum* infections of canaries and is also very active against *P. gallinaceum*. The present authors believe that its presence as an impurity is largely responsible for the activity of the related substance R63. This latter compound, as used by the authors, was considerably less active than pamaquin in both infections. The activity of a number of compounds related to the 4-aminoquinoline chloroquine [this *Bulletin*, 1946, v. 43, 708] and its 3-methyl derivative sontoquin, both of which were originally synthesized in Germany and later studied intensively in America, has also been investigated. It was found that the greatest activity was present in derivatives with the chlorine atom in position 7 in the quinoline nucleus as in chloroquine itself. Activity was reduced by the introduction of one (sontoquin) or two methyl groups. *J. D. Fulton*

TRYPANOSOMIASIS

i. FRIEDHEIM, E. A. H. **Melarsen Oxide in the Treatment of Human Trypanosomiasis.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 357–63.

ii. ——. **Mel B in the Treatment of Human Trypanosomiasis.** *Amer. J. Trop. Med.* 1949, Mar., v. 29, No. 2, 173–80.

iii. ——. **The Active Form of Tryparsamide, TPB, in the Treatment of Human Trypanosomiasis.** *Ibid.* 131–4.

i. Melarsen oxide is the trivalent analogue of the pentavalent arsenical, Melarsen [FRIEDHEIM, this *Bulletin*, 1941, v. 38, 634; WILLIAMSON and

LOURIE, *ibid.*, 1948, v. 45, 413]. It was believed by WEINMAN and FRANZ [*ibid.*, 1946, v. 43, 207] and by VAN HOOF [*ibid.*, 1947, v. 44, 1048] to be effective against late stage *gambiense* sleeping sickness, and FRIEDHEIM now reaches a similarly favourable conclusion.

The tests were carried out in the Bobo-Dioulassou district of the High Volta, and in the Gueckedou and Kissidougou districts of French Guinea. The drug was given to 54 patients, including 19 with pathological cerebrospinal fluids, and the author reports particularly on the results in the latter, more advanced cases. The course consisted of two series of seven daily intravenous injections of 1·5 mgm. per kgm. body weight, separated by a rest-period of one month; these are higher dosages than were used by WEINMAN and FRANZ and by VAN HOOF. There were no toxic effects.

Lymph glands and blood were cleared of trypanosomes within 24 hours, and they remained clear on weekly examination during the following two months. Trypanosomes disappeared from the cerebrospinal fluid within one week in all of nine cases in which they had been seen in the fluid at the start of treatment. The cerebrospinal fluid cell-count returned to normal within three weeks of the first series of injections in all of 13 cases which had started with abnormal fluids, and in nine of these the count had in fact already been reduced to normal after only a single week. The effect on protein values was slower; return to normal being noted in only four of nine cases one week after the end of the second series of injections (*i.e.*, seven weeks after the start of treatment).

Only five advanced cases were followed up for 4–10 months after the last injection. Although the cell count and protein-content reverted to normal in all five, they took 3–9 months to do so. (These cases were treated and observed by LE ROUZIC in Bobo-Dioulassou, where climatic and epidemiological conditions are very different from those of Gueckedou and Kissidougou, where the other observations were made.)

The author mentions that there are a number of compounds which are effective against the lymphatico-blood stage of infection, but once the central nervous system is invaded tryparsamide is the only drug which may save the patient; it is, however, an unsatisfactory compound in the early stages [a view widely held by French workers, for which there does not seem to this reviewer to be very much evidence]. Accordingly, mass treatment has to choose between (*a*) lumbar puncture of all patients, followed by the administration of a drug like pentamidine for early cases and the lengthy tryparsamide course for late cases—the method mainly favoured by French and Belgian workers, and (*b*) no routine lumbar punctures, all patients being treated as though the central nervous system were involved, by combinations of drugs such as antrypol and tryparsamide—as practised in a number of British West African territories. The author concludes that melarsen oxide is as good as, if not better than, tryparsamide for late cases with the additional advantages that a curative course of two series of injections lasts only six weeks as compared with seven months for tryparsamide, and that it is a satisfactory drug also for early cases.

(ii) As indications of the magnitude of the problems involved, FRIEDHEIM quotes that in French West Africa in 1946 the Sleeping Sickness Service examined 4·6 millions of the population of 16 millions, and detected 50,000 new cases, of whom 60 per cent. were in the second stage of infection. In the Belgian Congo in 1947, 80 per cent. of all second stage cases were said to be tryparsamide-resistant. There is need of a drug which can cure in all stages of the disease and in a short course of treatment.

Results are presented of treatment with a new compound, "Mel B", which the author describes as "an alkyl mercapto derivative of melaminylphenylarsenoxide containing trivalent arsenic". It is tolerated at significantly higher doses than melarsen oxide, thus allowing the individual dose to be doubled

and the duration of treatment to be shortened. The drug was tested in Bobo-Dioulassou and Gueckedou in 50 late cases of *gambiense* infection, including 20 with trypanosomes in the cerebrospinal fluid. It was given at a dosage of 2 to 4 mgm. per kgm. intravenously for 3 to 14 daily injections, either in a single series or in two series separated by a rest period. There were no signs of toxicity. Trypanosomes disappeared from the blood or glands within 24 hours, and were also no longer present in the cerebrospinal fluid in nine out of nine previously positive cases examined by lumbar puncture one week after treatment.

The patients were followed up for periods varying to a maximum of seven months, and changes in the cerebrospinal fluid cell-count and protein are presented in tabular form, case by case, in three groups, as follows :—

Group I.—Follow-up period averaged 108 days ; 20 cases in which the cell-count and protein-content had both returned to normal when last examined.

Group II.—Follow-up period averaged 78 days ; 23 cases in which the cell-count but not the protein had returned to normal when last examined.

Group III.—Follow-up period averaged 70 days ; 7 cases in which neither the cell-count (though much reduced) nor the protein had yet returned to normal when last examined.

The cell-count and protein-content may both be restored to normal within two weeks of treatment, but, as with other forms of treatment, the usual effect was for the protein-content to remain raised much longer than the cell-count. The author refers to the difficulty of deciding whether increase in the cerebrospinal fluid protein, in the absence of other abnormalities, is merely a residual effect or whether it presages a relapse, and further research on this point is recommended. " Thousands of former patients all over Africa continue to be treated with large amounts of arsenicals as a precautionary measure, although they are clinically cured and present no other change than a high albumen content. It is suggested that a qualitative analysis of the cerebrospinal fluid albumen may help to select the cases where further treatment is really required."

The recommended treatment course with Mel B for all stages of infection is two series of four intravenous injections at 3·6 mgm. per kgm. body weight, with an interval of one week between the two series.

(iii) As is well known, tryparsamide itself is relatively non-trypanocidal and it is only when this pentavalent arsenical is reduced to its trivalent form that the trypanocidal property emerges. Reduced tryparsamide is, however, much more toxic than tryparsamide, besides being a more unstable substance. These disadvantages have been overcome by a " method of stabilisation and detoxification of reduced tryparsamide, developed in this laboratory and to be described elsewhere ". The new product, designated " T.P.B." contains 21·6 per cent. trivalent arsenic.

The drug was administered to ten patients in the second-stage of *T. gambiense* infection, including two with trypanosomes in the cerebrospinal fluid. There were no toxic effects. Five patients were treated by mouth and five intravenously. Trypanosomes rapidly disappeared from glands, blood and cerebrospinal fluid after a single dose, either by mouth or intravenously.

A table shows changes in the cerebrospinal fluid in five cases given 7 to 16 doses by mouth and followed up for 7 to 162 days. The fluid was restored to normal, or near to normal, in all five cases.

There was no improvement in a patient (and in a guineapig) infected with tryparsamide-resistant trypanosomes.

[The precise chemical composition of melarsen oxide is stated, but not that of " Mel B " or of " TPB ". Publication of the results of chemotherapeutic trials of new drugs unaccompanied by such information is to be deprecated. The claims made for these three compounds are of considerable importance, and further information and investigation are clearly desirable.] *E. M. Lourie*

Sampath, A. & Little, P. **Cultivation of *Trypanosoma cruzi* in Liquid Media.** *J. Bacteriology.* 1949, Feb., v. 57, No. 2, 265.

The junior author, with Subbarow [this *Bulletin*, 1946, v. 43, 538] described a liquid medium for the cultivation of *Trypanosoma cruzi*. For two years, they have now been using a more enriched basal medium, with the use of which they are able to grow *T. cruzi* in the coagulum-free filtrate obtained by extracting fresh coagulum of rabbit red blood cells with basal medium.

The enriched medium has the following formula :—

%		
1...	...	Peptone (Difco)
1...	...	" Casamino acids "
0·5	...	Sodium chloride
0·2	...	Glucose
10 mgm.	...	β-Alanine
10 ,,	...	Glycine
2 ,,	...	Folic acid
2 ,,	...	Nicotinamide
2 ,,	...	Thiamine
2 ,,	...	Choline

Optional : 1 per cent. corn steep liquor, free of alkaline precipitate. (The corn steep liquor was adjusted to an alkaline pH, filtered, and neutralized before use. It prolonged the viability of cultures.)

This has been found better than the original medium for certain strains of *T. cruzi*. It may be used with the rabbit-blood coagulum already described or the medium may be activated by the addition of 10 gm. of semi-dry fresh coagulum per 100 cc. The whole is mixed in a Waring blender and filtered. The activated filtrate remains stable after autoclaving and may be kept in a refrigerator for several months. *H. J. O'D. Burke-Gaffney*

Borzone, R. A. El ojo mongólico y el xenodiagnóstico artificial en la investigación de la enfermedad de Chagas. (Nota Previa). [**The " Mongol Eye " in the Artificial Xenodiagnosis of Chagas's Disease.**] *Semana Méd.* 1949, Apr. 21, v. 56, No. 16, 527–8, 3 figs.

Launoy, L., Lagodsky, H. & Jeanpierre, C. Sur quelques caractères différentiels entre deux souches de *Trypanosoma brucei*. [**Some Differential Characters between Two Strains of *Trypanosoma brucei*.**] *C. R. Soc. Biol.* 1949, Jan., v. 143, Nos. 1/2, 6–8.

Harvey, S. C. **The Carbohydrate Metabolism of *Trypanosoma hippicum*.** *J. Biol. Chem.* 1949, May, v. 179, No. 1, 435–53, 2 figs. [34 refs.]

LEISHMANIASIS

Ramos e Silva, J. Leishmanides. Considerações sôbre a forma generalizada da leishmanides tegumentar Americana. [**Leishmanids—a Generalized Form of American Cutaneous Leishmaniasis.**] *Brasil-Medico.* 1949, Jan. 22 & 29, v. 63, Nos. 4/5, 23–6, 5 figs. English summary.

Multiple lesions of cutaneous leishmaniasis are usually the result of auto-inoculation by digital transfer or of multiple infections. Here the author

records the case of a man of 53 years with an initial espundia sore on the left leg, followed by two sores of the lip and chin, possibly, even probably, caused by auto-inoculation and digital transfer. These were succeeded by lesions on the neck, trunk (back and front) and arms, furunculoid in appearance, with a lymphangitis and adenitis. Wassermann reaction was negative and beneath the crusts of the lesions abundant leishmania could be found. These disseminated papulo-pustular lesions appeared about two months after the primary lesion. Though the facial sores were probably the result of auto-inoculation, the presence of lymphangitis and lymphadenitis indicates extension by the lymphatics and the wide dissemination may be ascribed to a spread by way of the blood-stream. *H. Harold Scott*

FEVERS OF THE TYPHUS GROUP

MEXICO. Primera Reunion Interamericana del Tifo. Mexico, D.F. 7–13 de octubre de 1945. [**The First Inter-American Conference on Typhus.**] 455 pp., numerous figs. 1947. Mexico.

This volume contains a collection of papers read at the First Inter-American Conference on Typhus, which was held at Mexico City in October 1945.

Most of the papers would have been of great interest if they had been published soon after the holding of the conference, but the great delay in publication is not so unfortunate as it would have been if the contributors had not published the substance of their articles elsewhere.

The papers on the distribution of the fevers of the typhus group in various countries of the American Continent will be of interest to students of the geographical distribution of the diseases. The name typhus is used in its broad sense by most of the contributors, and so includes the tick-borne disease which, though called by different names, is now regarded as being the same as Rocky Mountain spotted fever throughout the American Continent.

The list of authors is impressive; it contains such well-known names as Anigstein, Camargo, Castañeda, Cox, Craigie, Dyer, Macchiavello, Pinkerton, the late Col. Plotz, Soper, and Topping, but there is little in their contributions that has not been reviewed in this *Bulletin*.

In view of the controversy that has arisen in connexion with priority for the initiation of mass-dusting of fully clothed persons by insecticide dusts, a brief reference may be made to the paper by F. L. SOPER, F. S. MARKHAM, W. A. DAVIS and L. A. RIEHL on their Experience with Powders in the Control of Typhus in Italy, 1943 to 1945. These workers were members of the Rockefeller Foundation Typhus Team, and after experiments in Egypt early in 1943, which proved that insecticide powders could be used with success for mass delousing of clothing, they went on in July, 1943 to test MYL and DDT powders at the Maison Carrée Prison, Algiers, where they found that the powders could be satisfactorily applied with hand dusters or compressed-air units, without removing the clothing from the body. They state that this work was " very important since it was the basis of the proposal, made in the initial discussion with the Military Government Section of the A.F.H.Q., to undertake control of typhus fever in occupied Italy with louse powder alone." This proposal was put into effect with startling success in Naples in December, 1943, and although vaccination was also adopted in January, 1944, this came too late to have any significant influence on the course of the epidemic. The authors emphasize the ease with which louse infestation, and so typhus transmission, can be controlled in this way.

In view of the formerly held opinion that epidemics of louse-borne typhus in Mexico often originated from murine strains of rickettsiae which adapted themselves to louse transmission it is surprising to find hardly any mention of this hypothesis apart from a few references to the occurrence of "intermediate" strains. The general impression conveyed to the reader is that the human and murine strains are regarded as maintaining their own individuality and that the name murine typhus is accepted as being synonymous with flea-borne typhus.

The volume is attractively produced, and apart from a few misprints the synopses in English are good translations from the Spanish versions.

John W. D. Megaw

WEYER, F. Laboratoriumsinfektionen in Beziehung zu ätiologischen und epidemiologischen Fragen beim Fleckfieber und Wolhynischen Fieber. [**Laboratory Infections; their Bearing on the Aetiology and Epidemiology of Typhus Fever and Trench Fever.**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. [1949], v. 1. No. 1, 2–32. [Numerous refs.]

The author describes and discusses four cases of laboratory infection with rickettsiae; these occurred in 1947–48 and were detected by the finding of rickettsiae in lice which had fed on the patients in the course of their employment as blood donors to the insects. All the patients had already suffered from typhus fever.

The clinical features were in keeping with the diagnosis of atypical forms of trench fever; the rickettsiae were of the extracellular type, and were found by later feeding experiments with lice to persist for several months in the blood of the patients. In one case the lice fed at a later stage were found infected with the intracellular form of rickettsia which differs from the extracellular in being pathogenic for lice and mice. In another case a strain which was originally extracellular became intracellular after passage through mice.

The author discusses at length the nature of the infection and the significance of the findings in connexion with the aetiology and epidemiology of typhus fever and trench fever.

The infection may have been a late relapse of typhus fever, such as occurs in Brill's disease; or trench fever; or a mixed infection of typhus and trench fever.

The author suspects that in certain environmental conditions *R. prowazeki*, the intracellular form, may become transformed to the extracellular form, *R. wolhynica*, and *vice versa*. The discussion is too long for an adequate summary.

John W. D. Megaw

CHANG, N. C. **Slide Agglutination Test for Rapid Diagnosis of Typhus and Typhoid Fevers.** *Chinese Med. J.* 1948, Nov., v. 66, No. 11, 612–14. [14 refs.]

Slide-agglutination tests for typhus and typhoid fever are described. Details are given of the methods employed in the preparation of formolized suspensions of *Proteus OX19* and of typhoid (0–901) bacilli.

In each case positive agglutination within one minute was invariably observed with sera which reacted at 1–160 or over with the tube tests.

The suspensions are said to keep well for five months, even at room temperatures.

John W. D. Megaw.

GILBERT, A. Étude clinique de 118 cas de typhus exanthématique observés en 1945 à l'Hôpital Claude Bernard. [**Clinical Study of 118 Cases of Exanthematic Typhus treated at the Claude Bernard Hospital in 1945.**] *Rec. Travaux Inst. Nat. Hyg.* Paris. 1948, v. 2, 417–31.

Of the 94 patients treated during the active stage of their illness 85 had contracted the infection in Germany. In patients under 40 the fatality rate was 4·5 per cent.; in those over 40 it was 17 per cent.

The clinical features were of the usual type. The Weil-Felix reaction was positive at low titres in about half of the cases by the sixth day, and in nearly every case at high titre from the tenth day onwards; in cases tested after recovery it was found to have become negative by the 23rd to the 41st day. The rickettsia-agglutination test became positive earlier than the Weil-Felix; in one case the titre was 1–800 on the first day; from the sixth day it was positive at titres of 1–200 to 1–800 in 85 per cent. of the cases. The author mentions as a possible drawback the persistence of the reaction after recovery; he suspects that positive reactions due to previous attacks may sometimes occur.

The Widal reaction was positive in two-thirds of the cases at titres of 1–50 to 1–200. *John W. D. Megaw*

GIROUD, P., CIACCIO, G. & VARGUES, R. Valeur antigène et pathogène du précipitat desséché obtenu par l'alcool méthylique à basse température et provenant du poumon de lapin infecté par des rickettsies. [**The Antigenic and Pathogenic Potency of a Dried Precipitate obtained from Rickettsia-infected Rabbit Lung by Extraction with Methyl Alcohol at Low Temperature.**] *C. R. Soc. Biol.* 1948, Dec., v. 142, Nos. 23/24, 1476–8.

A suspension of the lungs of rabbits infected with *Rickettsia prowazeki* was centrifuged at low speed; to the supernatant fluid methyl alcohol was added making an alcoholic strength of 20–25 per cent. The mixture was reduced to a temperature of —8°C., which was reached within two hours. The precipitate was separated by high-speed centrifugation and desiccated; during the whole process the temperature was not allowed to rise above 0°C.

With the rabbit intradermal test the antigen caused a relatively slight local reaction, but it produced a degree of immunity in guineapigs corresponding to that obtained with corresponding doses of formol-killed rabbit-lung antigen.

The authors suggest that if the procedure results in the preservation of a trace of the virulent antigen and the whole of the stabilized antigen it may be found suitable for the production of a satisfactory vaccine.

John W. D. Megaw

GIROUD, P. & CIACCIO, G. Valeur antigène d'extraits en sérums de poumons de lapins infectés de *Rickettsia prowazeki* prouvée par l'agglutination des rickettsies. [**The Potency of an Antigen obtained by Extraction with Serum from the Lungs of Rabbits infected with** *Rickettsia prowazeki*.] *C. R. Soc. Biol.* 1948, Dec., v. 142, Nos. 23/24, 1479–80.

A suspension of the lung of a rabbit infected with *R. prowazeki* was added to normal horse serum. The mixture was kept for 5–18 hours at about 4°C. Supernatant fluid obtained by centrifugation was injected into rabbits, whose sera, tested 10 and 15 days afterwards, were found to agglutinate typhus rickettsiae at a titre of 1–640; this titre was the same as was observed in rabbits injected with corresponding doses of fluid prepared in the same way except that extraction was by a 0·8 per cent. solution of sodium chloride instead of horse serum.

Heating the horse serum to 56°C. for 75 minutes did not affect the potency of the antigen, nor did keeping the prepared fluid at 4°C. for 24 hours, but the use

of formolized horse-serum produced a reduction in the rickettsia-agglutination titre of the fluid by about one-half. *John W. D. Megaw*

SERGENT, Ed., BÉGUET, M., PARROT, L. & HORRENBERGER, R. La prophylaxie du typhus exanthématique en temps d'épidémie et dans les périodes inter-épidémiques en Algérie. [**The Prevention of Exanthematic Typhus in Epidemic and Interepidemic Periods.**] *Arch. Inst. Pasteur d'Algérie.* 1949, Mar., v. 27, No. 1, 1–6.

The authors were associated with the field experiments which formed the basis of the successful control of the famous Naples epidemic of 1943–44. They mention the trials of MYL and DDT carried out in collaboration with the Rockefeller Foundation team headed by F. L. SOPER; at the Maison Carrée prison and in a rural area near Algiers during the first half of 1943, and state that "The Pasteur Institute of Algeria conceived the idea (*imagina*) of blowing the powder under the clothing."

The methods recommended in Algeria are (1) During epidemics, vaccination with killed vaccines and dusting all persons exposed to risk of infection, employing insecticide powders, and (2) During interepidemic periods the yearly vaccination of the inhabitants of endemic areas, without using insecticide powders. The omission of dusting except during epidemics is presumably based on the principle of making the best use of the available staff and materials; apart from this consideration it would appear advisable to maintain louse control at all times in endemic areas.

Vaccination with a single dose of the killed vaccine of Durand and Giroud is recommended; it is carried out simultaneously with smallpox vaccination and antituberculosis inoculation with B.C.G., so that the health staff can deal with the prevention of three great diseases at the same time. [See also this *Bulletin*, 1949, v. 46, 539.] *John W. D. Megaw*

CHAUDHURI, R. N. & CHAKRAVARTI, H. **Typhus in Calcutta.** *Indian Med. Gaz.* 1949, Feb., v. 84, No. 2, 43–51, 3 figs. [15 refs.]

The author gives a good clinical description of 25 cases of "typhus fever" studied in a Calcutta hospital during the previous 32 months. Four of the cases were diagnosed as "murine typhus (OX19)", and 21 as "mite typhus (OXK)". There were two deaths. The patients were closely observed and the clinical features as described were in keeping with the diagnosis of fevers of the typhus group. Two of the patients had eschars; seven had enlarged glands in the neck. The white-cell count was usually within normal limits. There was hypoprotinaemia in most of the cases, the defect being in the albumin fraction.

Among the cases of the "OXK type" one gave a negative reaction in each of four weekly Weil-Felix tests, though rickettsiae were recovered from the blood; this was a case of laboratory infection resulting from the bite by a mouse which was being inoculated with a "typhus emulsion." There was a whitlow-like eschar at the site of the bite.

In the other OXK cases titres of 1–100 to 1–12,800 were observed.

John W. D. Megaw

BRICEÑO-IRAGORRY, L. Estudio sobre 4,203 reacciones de Weil-Felix en sueros de febricitantes de la zona de Caracas. [**Study of 4,203 Weil-Felix Reactions in Cases of Fever in the Caracas Area.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Apr., v. 10, No. 2, 309–17.

The 4,203 sera were from persons suspected of having typhoid fever. During the five-year period, 1940–1944, in which the tests were carried out 41 cases of

murine typhus were diagnosed by the reaction ; these are discussed separately. The sera were tested first by a rapid slide method and the positives were further tested by the standard method.

The number of sera reacting with *Proteus OX19* at titres of 1–40 or over was 365 (8·4 per cent.). Reactions at titres of 1–160 and 1–320 are specially discussed. There were 31 (0·73 per cent.) at the former titre and 25 of these also reacted at titres of 1–40 to 1–320 against an O strain of typhoid bacilli, leaving only six cases in which the Weil-Felix reaction could not be explained either as a para-agglutination in cases of typhoid fever or as a typhus reaction. In all the 7 cases in which the titre was 1–320 the Widal reaction was also positive at titres of 1–160 to 1–320, and the diagnosis of typhoid fever was established so the Weil-Felix reactions were regarded as para-agglutinations.

In the 41 cases of murine typhus already mentioned the Weil-Felix titres ranged from 1–200 to 1–10,000, and only one gave a positive Widal reaction against an O strain, of typhoid, and that was at a titre of 1–40. There were a few reactions against an H strain, against paratyphoid B and C, but never at a titre higher than 1–80.

The conclusions reached were—(1) Weil-Felix titres of 1–80 or less have no diagnostic significance unless the titre is found to be rising ; (2) A titre of 1–160 in the absence of a positive Widal reaction is suspicious and calls for further investigation. (3) A titre of 1–320, unless accompanied by a positive Widal reaction, is regarded as diagnostic ; (4) In typhus fever there is little tendency to the development of typhoid agglutinins, whereas in typhoid fever there may be a pronounced tendency to the production of agglutinins against *Proteus OX19*.

[The last conclusion is contrary to the experience of most of the other workers on the subject.] *John W. D. Megaw*

Varela, G., Pérez-Rebelo, R., Roch, E. & Olarte, J. Exploración de tifo en ratas de la ciudad de Mexico, por medio de la fijación del complemento con rickettsias y aglutinación con *Proteus OX19*. [**Survey of the Prevalence of Typhus Infection of Rats in Mexico City, by Complement-Fixation and Weil-Felix Tests.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, June, v. 9, No. 2, 139–44. English summary.

Complement-fixation tests, with the use of murine antigen, were carried out on 1,376 rats trapped in Mexico City between March and September, 1948. In 9·7 per cent. of these, positive results were observed. In most cases the reactions with epidemic antigen were also positive, but always at titres of one-half or less when compared with the reactions against murine antigen.

In another series of 1,157 rats Weil-Felix tests were carried out. Against *Proteus OX19* there were 12·2 per cent. of positives, and in about one-third of these there were positive reactions against *Pr. OXK* or *Pr. OX2* or both. Against *Pr. OXK*, 7·9 per cent. of the rats gave positive reactions and against *Pr. OX2*, 3·5 per cent. reacted ; in both of these groups about one-half of the reacting animals were positive also with one or both of the other *Proteus* strains. Altogether 18·7 per cent. of the rats agglutinated one or more *Proteus* strains at titres of 1–80 or over. *John W. D. Megaw*

Krishnan, K. V., Smith, R. O. A., Bose, P. N., Neogy, K. N., Roy, B. K. G & Ghosh, M. **Clinical Features and Laboratory Diagnosis of XK or Mite-borne Typhus as observed in 102 Cases in the Barrackpore Area.** *Indian Med. Gaz.* 1949, Feb., v. 84, No. 2, 33–9, 3 charts.

This is the first of a series of four papers by the Bengal Typhus Enquiry team, based on the All India Institute of Hygiene, Calcutta.

During the years 1946–48, 102 cases occuring at Barrackpore, near Calcutta, were diagnosed as " typhus fever ". The case-fatality rate was 3·0 per cent.

In 64 of the cases the diagnosis was confirmed by the Weil-Felix test and by isolation of rickettsiae from inoculated animals. Serologically 72 per cent. of the cases were of the XK type ; 19 per cent. were of the " X19 (murine) type " and 9·0 per cent. of the X2 type.

It was not possible to differentiate the three serological types on clinical grounds. A description is given of the clinical features of the XK cases ; 80 per cent. of these were mild and no eschar was detected in any of them ; 20 per cent. were severe, in 5 of them there was an eschar. A rash was seen in 7·0 per cent. of the mild cases, and in 75 per cent. of the severe. In the mild cases the diagnosis of a typhus-group fever was usually impossible on purely clinical grounds.

In the X19 cases the Weil-Felix titre always rose to 150 or over, but guineapig inoculation, carried out in some of the cases, never caused a Neill-Mooser reaction.

In the XK cases the Weil-Felix reaction was completely negative in 10 per cent. ; it reached titres of only 125 or 1–50 in 25 per cent. ; in 65 per cent. the titre was 1–100 or over.

There were 7 cases of the X2 type, all of which had titres of 1–125 or over. and all reacted also with OXK or OX19 at titres of 1–25 or 1–50. The authors rightly suggest that this type needs to be properly investigated, especially as animal inoculation " has not been very helpful ".

Washed blood cells from the XK cases were used for the inoculation of white mice, in which ascites always occurred in the positive cases, whereas " by no other strain studied was it caused ". Inoculated mice, when positive, always yielded visible rickettsiae from peritoneal scrapings taken about the 8th day.

Mice inoculated with the blood of one of the X2 patients reacted in the same way as those inoculated from XK patients so that " this strain was assumed to be one of XK and not of X2 ", whereas blood of another X2 patient caused an inapparent infection in a mouse and guineapig, but a strain of rickettsia was isolated by subinoculation with spleen and brain material, and this was easily passaged through guineapigs. The comment made is that " this strain may be considered to be an X2 strain of this area ".

Suitable antigens were not available for complement-fixation tests, which, however, were not regarded as being very necessary except in connexion with the X2 cases.

[Few workers on the typhus fevers would regard the complement-fixation tests as superfluous in such conditions ; it would be easy to submit sera to one of the American laboratories specializing in the test.

In view of their own findings it is surprising that the authors have gone to such lengths in their attempt to correlate the classification based on the Weil-Felix response with the recognized classifications. The OX19 type includes not only louse-borne and flea-borne typhus, but also many cases of tick-borne typhus ; 35 per cent. of the present cases classed as XK typhus did not give significant reactions with *Proteus OXK*, and one case giving an X2 reaction is said really to belong to the XK group. Boyd who first employed the classification based on the Weil-Felix response never claimed any significance for this except as a statement of the fact that sera from various parts of India gave certain responses ; indeed he was not classifying the types of disease, but only the types of reaction.] *John W. D. Megaw*

KRISHNAN, K. V., SMITH, R. O. A., BOSE, P. N., NEOGY, K. N., ROY, B. K. G. & GHOSH, M. **The Breeding and Maintenance of *Trombicula deliensis* in the Laboratory for Experimental Purposes.** *Indian Med. Gaz.* 1949, Feb., v. 84, No. 2, 39–41, 1 pl.

This paper will be read with great interest by all workers on the vectors of mite-borne typhus. The authors are to be congratulated on their remarkable success in breeding *Trombicula deliensis* in the laboratory.

Ingenious methods are described by which three complete generations of the mites have been reared, starting from a colony collected from local rats.

A few mites collected in June 1948 were still alive and breeding five months later. A brief description of all the stages in the life cycle is given, and is illustrated by an excellent plate showing photomicrographs of each stage. In the following list of the stages the approximate duration of each, in the conditions described, is shown in brackets. Egg (7 days) ; deutovum (7 days) ; larva (3–5 days) ; nymphochrysalis (7 days) ; nymph (7–14 days) ; imago-chrysalis (7 days) ; and adult.

The special importance of this study is that for the first time it places at the disposal of other workers a method of obtaining laboratory-bred mites in sufficient numbers for employment in transmission experiments.

The initial success in rearing the larval mites was due to the adoption of the method used by WHARTON and CARVER who fed nymphs of *Neoschöngastia* mites on insect eggs [see this *Bulletin*, 1946, v. 43, 1079]. For details of the authors' methods the original paper must be consulted.

John W. D. Megaw

KRISHNAN, K. V., SMITH, R. O. A., BOSE, P. N., NEOGY, K. N., ROY, B. K. G. & GHOSH, M. **Transmission of *Rickettsia orientalis* by the Bite of the Larvae of *Trombicula deliensis*.** *Indian Med. Gaz.* 1949, Feb., v. 84, No. 2, 41–3.

As a happy sequel to their success in breeding mites in the laboratory, the authors are now able to report that they have transmitted *Rickettsia orientalis* from mouse to mouse in the laboratory by the bites of larval *Trombicula deliensis* which were the progeny of larvae infected by feeding on infected mice.

Five of the eight mice on which infected larvae had fed became infected ; the infection was inapparent but was demonstrated by the recovery of strains from mice inoculated with brain suspensions of the fed mice.

The three mice which did not become infected had been bitten by 11 to 30 larvae ; in the successful cases the mice had been bitten by 38 to 78 larvae. No natural infection could be detected in any mice of the strain used in the above experiments.

The paper contains a hint that experiments on the transmission of infection to human volunteers may be contemplated by the authors.

John W. D. Megaw

KRISHNAN, K. V., SMITH, R. O. A., BOSE, P. N., NEOGY, K. N., ROY, B. K. G. & GHOSH, M. **Epidemiological Observations on XK or Mite-borne Typhus in Barrackpore, Bengal.** *Indian Med. Gaz.* 1949, Feb., v. 84, No. 2, 63–8, 3 charts. [12 refs.]

This is a description of the epidemiological features of the fevers of the typhus group in Barrackpore, a cantonment town near Calcutta.

The disease was most prevalent during the rainy season, May to October ; this was also the season of greatest abundance of *Trombicula deliensis*.

Most of the persons affected were workers or campers in the scrub, jungle, or fields. *T. deliensis* mites were found in large numbers on 24 per cent. of the local *Rattus rattus*, and 20 per cent. of the highly infested rats were found infected with *Rickettsia orientalis*.

[The authors mention the case of laboratory infection described in the preceding paper by CHAUDHURI *et al.* (above), and state that the blood showed agglutinins for OXK ; this is probably a mistake because the physicians in charge show the reaction as having been negative in tests made during each of the four weeks of the illness, and they add that this result shows " the unreliability of this non-specific test."] *John W. D. Megaw*

BROWNING, H. C. & KALRA, S. L. **Scrub Typhus subsequent to "Fulton" Vaccine and Investigation of the Infected Site.** *Indian J. Med. Res.* 1948, Oct., v. 36, No. 4, 279–90.

The greater part of this paper consists of a description of an epidemiological survey of an infected site at Palel in the Manipur State situated between Assam and Burma. There were 17 cases, one of which was fatal, of scrub typhus among 261 members of a Pioneer Force, camped on the site during the months July to September, 1945. The survey was carried out during the months September to November of the same year ; it is a good example of the kind of investigation found by experience to be most suitable in suspected areas. Rats in cages were placed at different points as baits for larval mites ; soil samples were searched ; local rodents and other animals were captured and tested for infection by mouse inoculation.

Four strains of the rickettsia of scrub typhus were recovered from rats (a variety of *Rattus rattus*) ; three of the strains were recovered from the blood of the rats. One strain was recovered from four *Hydromys humei*, one strain from the only tree shrew (*Tupaia belangeri belangeri*) which was examined, and one strain from one of the twelve specimens of field mice caught in the area. Four strains were recovered from 20 batches of mites collected from rats, and one strain from a mite found attached to a patient. *Trombicula deliensis* was the only species of mite present in all the batches from which infection was isolated. A strain was recovered from the blood of one of the authors (H. C. Browning), whose attack is described in detail.

A different species of rickettsia was recovered from ticks (*Haemaphysalis leachi*) ; this strain was found to be immunologically identical with the rickettsia of Rocky Mountain spotted fever, but its virulence for guineapigs was very low. [This is a significant observation, it shows that immunologically identical rickettsiae of tick-borne typhus may differ sharply in their virulence for guineapigs.]

The attack from which one of the authors suffered is of special interest because the patient had received three doses of the " Fulton " vaccine four-and-a-half months before the onset ; the attack must have been severe, there was delirium and incoherence of speech for several days ; the fever lasted 13 days and there were minor rises of temperature on the 15th and 18th days. Serum taken on the 18th day was sent to Dr. Topping at Bethesda, U.S.A., and was reported as having a complement-fixation titre of 1–512 against Karp antigen, and a titre of 1–32 against Gilliam antigen. The strain isolated from the patient gave complete cross-immunity with the other strains of *R. tsutsugamushi* isolated in the area. The authors conclude that the course of the disease had not been modified by vaccination, but they believe that the other evidence available on the subject suggests that the vaccine has some protective value, though this is short-lived so that it is advisable to follow

the advice of FULTON and JOYNER [this *Bulletin*, 1946, v. 43, 435] who recommend that " booster " doses should be given every three months.

The authors also recommend that in view of the immunological differences found to exist between strains from different areas vaccines should be polyvalent.

The only precaution taken by the patient while working in the infected area was a daily hot bath with soaping and scrubbing of the skin within two hours of each visit to the suspected site. The authors' comment is that either this treatment does not remove attached mites, or mite attachment for less than six hours can convey infection, or mites remain on the clothing for two to six hours and then can attack. *John W. D. Megaw*

KOUWENAAR, W. & ESSEVELD, H. **The Nature of Immunity against Scrub Typhus in Guinea-Pigs.** *Documenta Neerlandica et Indonesica de Morbis Tropicis*. Amsterdam. 1949, Mar., v. 1, No. 1, 34–40. [34 refs.]

In a large series of experiments carried out in North Sumatra, the authors found that guineapigs convalescent from infection with 14 different strains of *R. orientalis* remained immune against challenge with homologous or heterologous strains for long periods, in one case up to 708 days.

Only one strain, isolated in Sumatra, differed from the others in failing to immunize against the other strains. The authors refer to the findings by BENGTSON [this *Bulletin*, 1945, v. 43, 551] and other workers of differences in the antigenic structure of various strains of *R. orientalis*.

Attempts to demonstrate the presence of protective antibodies in the sera of convalescent patients and guineapigs gave unsatisfactory results ; large daily injections of the sera, started one or two days before inoculation, failed to modify the illness in guineapigs. When infected material was mixed with the serum before inoculation the fatality rate was 49 per cent., with similar doses mixed with normal serum it was 72 per cent., so there seemed to be some attenuation of the virulence of the infection.

The persistence of viable rickettsiae in the recovered guineapigs was most easily demonstrable by inoculation with spleen substance ; second best was blood ; but brain, testicular tissue, and urine, gave more negative than positive results in the tests carried out 26 or more days after the end of the fever.

The immunity is believed to be an " infection immunity " of the type described by SERGENT [*prémunition*]. The relatively brief immunity observed in man and monkeys is believed to be associated with the disappearance of rickettsiae from their bodies soon after recovery from the illness.

John W. D. Megaw

UNITED PLANTING ASSOCIATION OF MALAYA. **Scrub Typhus and its Prevention.** Prepared by the Scrub Typhus Research Unit at the Institute for Medical Research at the Request of the United Planting Association of Malaya. 8 pp. Kuala Lumpur.

This pamphlet of eight pages was prepared by the Scrub Typhus Research Unit at Kuala Lumpur at the request of the United Planting Association of Malaya. It is a model of what such a pamphlet ought to be, containing as it does in simple language what every layman in Malaya needs to know and needs to do in connexion with the prevention of scrub typhus.

The nature and manner of infection are described and the reader is told how to recognize the vectors by finding them as reddish or orange-coloured specks in the ears of infested rats. The harmless mites are described as being white or yellowish, and the mites that cause scrub itch in Malaya as bright scarlet in colour. As a rule of thumb it is advised that if half or more of the

rats trapped in an area are found infested, steps must be taken to deal with the area in consultation with the officers of the Research Unit.

A point of interest is the statement that the available supply of chloromycetin is so small that the drug can be used only for the very urgent cases. It is also stated that the supply of vaccine produced as a wartime emergency measure is exhausted.

The chief measures of prevention mentioned are the treatment of clothing with dibutyl phthalate ; spraying dangerous areas, marked down for clearance on the following day, with crude oil at the rate of 40 gallons to the acre ; smearing the legs of labourers with the same oil ; and employing labourers who have already had an attack of the disease. Gammexane applied as a dust at the rate of one pound to the acre is said to be " probably an effective agent ", which, however, should not be applied without expert advice.

Warning is given that rat destruction should not be employed for the immediate control of infection, though it is valuable as a long-term policy.

John W. D. Megaw

Audy, J. R. **Some Ecological Effects of Deforestation and Settlement.** Reprinted from *Malayan Nature J.* 1948, Dec., v. 8, No. 4, 178–89, 3 figs.

This paper is of chief interest to naturalists, but it contains a significant reference to the special risk of scrub-typhus infection in the " fringe habitats " which are narrow zones at the periphery of forest clearings and which provide a combination of conditions favourable to the fauna of the forest as well as of the clearings. Hence the richness of the fringe habitats in the hosts of the mite vectors of scrub typhus.

John W. D. Megaw

Harrell, G. T. & Aikawa, J. K. **Pathogenesis of Circulatory Failure in Rocky Mountain Spotted Fever. Alterations in the Blood Volume and the Thiocyanate Space at various Stages of the Disease.** *Arch. Intern. Med.* 1949, Mar., v. 83, No. 3, 331–47, 13 figs. [Refs. in footnotes.]

Systematic studies by biochemical and other methods were carried out in 13 cases of Rocky Mountain spotted fever, all of whom were given supportive treatment ; in six of the cases antiserum or para-aminobenzoic acid, or both, were also given. The paper is illustrated by a set of elaborate charts showing the changes occurring in such features as pulse rate, blood pressure, plasma volume, thiocyanate space, total serum protein, serum albumin, etc.

The authors discuss the findings in each case ; some of the conclusions reached were :—There is an increased permeability of the capillaries, especially during the second week of the rash ; this is believed to be associated with the antigen-antibody reaction, in the course of which a histamin-like body is produced, causing an escape of fluid and proteins from the blood to the cells and tissues of the body, and oedema. The maintenance of circulating proteins by feeding on a high-protein diet is recommended in preference to transfusion. In two cases the unnecessary parenteral administration of serum albumin or plasma caused an increase in plasma volume and myocardial circulatory failure.

The administration of para-aminobenzoic acid or antiserum did not prevent circulatory changes. The excessive administration of fluids may precipitate myocardial failure.

The general impression conveyed to the reader is that indiscriminate parenteral treatment is more likely to do harm than good, and that patients who are given a generous diet, well supplied with high-grade proteins, will rarely need transfusions of serum, plasma, or whole blood. The authors'

warning against giving excessive amounts of fluid should not deter physicians from giving adequate quantities, especially in the early stages of the illness.

John W. D. Megaw

HARDY, S. M. **A Review of Preliminary Clinical Studies on Aureomycin, a New Antibiotic Agent.** *Bol. Asoc. Med. de Puerto Rico.* 1948, Dec., v. 40, No. 12, 347–50. [14 refs.]

This is a review of 14 papers (of which 9 are said to be " in the press " or " to be published ") dealing with aureomycin. The drug is said to be particularly indicated in (1) the rickettsial diseases—tick fever, typhus, lymphopathia venereum, Q fever, psittacosis, ornithosis, and certain bacterial and viral eye infections [this is the author's classification] ; (2) primary atypical pneumonia ; (3) genito-urinary tract infections due to penicillin-fast or streptomycin-fast organisms ; (4) acute and chronic brucellosis ; (5) streptococcus or staphylococcus or pneumococcus infections, especially those resistant to penicillin or streptomycin.

The usual method of administration is by the mouth, in doses of 25–100 mgm. per kgm. daily, for five to fourteen days. Parenteral injections are reserved for fulminating infections ; the dose recommended is 2–10 mgm. per kgm. daily, but this " may be too low ".

Verbal reports of two cases of death attributed to treatment are mentioned ; one was apparently due to anaphylactic reaction after intravenous treatment ; the other was with " an allegedly Hersheimer type of reaction " in a case of brucellosis.

John W. D. Megaw

ANIGSTEIN, L., WHITNEY, Dorothy M. & BENINSON, J. **Aureomycin : Protective Effect in Experimental Rocky Mountain Spotted Fever and Typhus with particular reference to Intermittent Treatment.** *Texas Reports on Biol. & Med.* 1949, v. 7, No. 1, 96–110.

By a series of experiments on guineapigs inoculated intraperitoneally with *Rickettsia rickettsi* the authors have confirmed the findings already reported by WONG and COX (*Ann. New York Acad. Sci.*, 1948, v. 51, 290) and other workers, including themselves, with regard to the powerful anti-rickettsial action of aureomycin.

In the present experiments it was found that intermittent treatment with doses of 1·0 to 3·0 gm. of the drug given every two or three days gave as good results as similar doses given daily. The intermittent treatment had less effect in preventing the development of high complement-fixation titres in the animals and so presumably interfered less with the production of immunity, but the recovered guineapigs were found immune when challenged with homologous rickettsiae even when the intermittent dosage had not been sufficient to cause complete suppression of the signs of infection.

John W. D. Megaw

DE MAGALHÃES, O. & ROCHA, A. Subsidio ao melhor conhecimento do tifo exantemático neotrópico no Brasil. Presença do virus no leite. [**Contribution to the Better Knowledge of the Neotropical Typhus of Brazil.**] *Mem. Inst. Oswaldo Cruz.* 1948, Mar., v. 46, No. 1, 269–83, 3 figs. English summary.

The authors state that they have demonstrated the presence of the " virus of exanthematic neotropical typhus " [presumably *Rickettsia rickettsi*] in the milk of a goat which, three days previously, had been inoculated intraperitoneally with a strain of the infection. The only sign of disease in the goat itself was a positive group reaction with the Weil-Felix test. The goat had been

inoculated with the same strain seven months previously, and had then shown no reaction except the positive response to the Weil-Felix test. The authors claim to have already demonstrated the transmission of infection to the dog by feeding on infected material [this *Bulletin*, 1943, v. 40, 300] so they conclude that the milk of apparently healthy goats may be a source of infection to children, even infants in arms; and state that "we have many such cases on record". *John W. D. Megaw*

DYER, R. E. **Q Fever. History and Present Status.** *Amer. J. Pub. Health.* 1949, Apr., v. 39, No. 4, 471–7. [66 refs.]

This is the first of a series of four papers on Q fever read at a meeting of the American Association of Public Health in November, 1948. It contains an excellent summary of the history of the disease. The bibliography containing 66 references adds greatly to the value of the paper. The name Q fever is often assumed to be an abbreviation of Queensland fever, but the author has been informed by Derrick that the letter Q stands for Query and that the name was given because he was at a loss to find a suitable descriptive title.

The authors of this and the following three papers have adopted the name *Coxiella burneti* instead of *Rickettsia burneti*, and so have accepted the view of PHILIP, who in 1943 [this *Bulletin*, 1948, v. 45, 424] expressed the opinion that the organism belonged to a different genus from *R. prowazeki* and *R. mooseri*.

It remains to be seen whether workers in other parts of the world will readily accept the necessity for this change of name. *John W. D. Megaw*

BELL, E. J., PARKER, R. R. & STOENNER, H. G. **Experimental Q Fever in Cattle.** *Amer. J. Pub. Health.* 1949, Apr., v. 39, No. 4, 478–84. [11 refs.]

The experiments described in this paper have already been reported, or will shortly be reported, in greater detail.

IRONS, J. V., MURPHY, J. N., Jr., RICH, A. B. & HILL, A. E. **Q Fever Survey in Southwest Texas.** *Amer. J. Pub. Health.* 1949, Apr., v. 39, No. 4, 485–91. [12 refs.]

In a survey in Texas the authors have found that the sera of about 5·0 per cent. of slaughter-house workers at San Antonio, Texas, contained complement-fixing antibodies for Q fever. They have confirmed the finding of Q fever rickettsiae in raw milk, and have found complement-fixing antibodies in sera of sheep and goats at a ranch where a case of Q fever occurred.

John W. D. Megaw

STRAUSS, E. & SULKIN, S. E. **Q Fever. Complement-Fixing Antibodies with *C. burnetii* Antigens in various Geographic Areas and Occupational Groups in the United States.** *Amer. J. Pub. Health.* 1949, Apr., v. 39, No. 4, 492–503. [23 refs.]

The results of complement-fixation tests, carried out on groups of persons in different parts of the U.S.A. were as follows:—

Titres of 1–8, or over, against Q fever antigens were observed in 8·0 per cent. of 1,433 sera from meat packers at Fort Worth, Texas; in 10·2 per cent. of 1,033 sera sent for syphilitic tests to the Dallas, Texas, laboratory; and in 7·9 per cent. of 175 unselected sera from Amarillo, Texas.

Smaller percentages of positive reactions occurred in sera from other localities:—0·7 per cent. in packing-house workers at Austin, Minnesota;

1·1 per cent. in sera from a Boston laboratory ; 2·1 per cent. in blood donors ; 2·0 per cent. in dairy workers of Dallas, Texas, and 2·0 per cent. in sera from Portland, Oregon.

An interesting point arises in connexion with the syphilitic sera from Dallas ; positive results occurred in 15·9 per cent. of the sera giving positive or doubtful reactions for syphilis, and in only 6·6 per cent. of negative sera. The question arises whether the reaction is always strictly specific. Mention is made of the finding by Robbins *et al.* that patients infected in Italy gave positive responses to an Italian strain of antigen, and negative responses to an American strain. In the present study the less sensitive American strain was used, and it is suggested that a larger number of positive reactions would have occurred if the Italian strain had been employed. *John W. D. Megaw*

Denlinger, R. B. **Clinical Aspects of Q Fever in Southern California ; a Study of 80 Hospitalized Cases.** *Ann. Intern. Med.* 1949, Mar., v. 30, No. 3, 510–27, 4 figs. & 1 chart.

The author has analysed the signs and symptoms observed in 80 cases of Q fever treated at various hopsitals in South California.

All were confirmed by complement-fixation tests. In 30 cases no history of exposure to even a suspicious source of infection was obtained.

The most frequent symptoms were as follows. Figures in brackets are percentages. Fever (100) ; chilliness (83·7) ; malaise (93·7) ; cough (62·5) ; anorexia (53·6) ; chest pain (36·2) ; nausea (32·5) ; profuse perspiration (30) ; vomiting (26·2) ; rigors (15). The onset was sudden ; severe and persistent headache was very common.

The most common physical findings were :—Fever (100) ; " acutely ill " (81·5) ; relative bradycardia (67·5) ; pulmonary râles (58·7) ; dullness on percussion and altered breath sounds, (26·2, each) ; pharyngeal injection (37·5) ; stiff neck (25) ; stupor (17·5) ; confusion (16·2) ; lymphadenopathy (16·2).

The fever tended to be continued for an average period of 10 days ; the total duration of the fever was 5–12 days in 65 cases and 13–20 days in the rest. The termination was by lysis.

The leucocyte count was very variable, but in most cases there was a slight degree of polymorphonuclear leucocytosis and lymphocytopenia.

The usual X-ray finding, as observed in 77 patients, was a segmented or lobar consolidation, most often in the lower lobe and least often in the upper lobe. Patchy infiltration and multiple areas of involvement of the lung were infrequent. In 12 cases no sign of infiltration was detected.

Recovery was usually rapid and complete. Relapse occurred in two cases, 6 and 8 weeks, respectively, after the illness.

No definite benefit was observed from treatment by penicillin, sulphonamides, streptomycin, or para-aminobenzoic acid. *John W. D. Megaw*

DENGUE AND ALLIED FEVERS

Ishii, N. **Studies on Dengue Fever. I. Studies on Dengue Virus and Immunity. (2).** *Japanese Med. J.* 1948, June, v. 1, No. 3, 228–38, 2 charts. [12 refs.]

This paper is the second part of a report on studies of dengue fever carried out in 1942–44. The first part was reviewed in this *Bulletin*, 1949, v. 46, 138.

The author describes the preparation of a formolized vaccine from a strain of the virus exalted in virulence by a series of passages from a natural human

strain which was transferred first to a rabbit or mouse, then to a human volunteer and finally to mice, which became severely affected. The virus has been maintained by serial passage through mice for four years.

A number of persons received three doses of the vaccine before migrating to infected areas in the Far East ; the presence of immune bodies in the sera of the immunized persons was shown by mouse-protection tests. One of five vaccinated persons who went to Sumatra had " a slight symptom of dengue " three months later, the others remained free from symptoms although a dengue " endemic " occurred among non-immunized persons. In New Guinea a number of non-immunized persons contracted typical dengue during three months of residence, but none of the ten immunized was attacked.

The evidence of the production of a worth-while immunity is not convincing.

John W. D. Megaw

RABIES

JAUJOU. L'infection rabique en Corse au cours de l'année 1946. [**Rabies in Corsica during 1946.**] *Bull. Acad. Nat. Méd.* 1948, v. 132, Nos. 7/8, 128.

The epidemic of animal rabies described in this paper occurred in Corsica, from which the disease had been absent since 1932. Introduced by dogs accompanying soldiers, who had crossed from North Africa where rabies is endemic, the infection appeared first between April and October in 1944, reappeared in April 1945 and, after remaining latent for some months, flared up and spread rapidly until the end of 1946. All kinds of livestock were involved in the epidemic, the infection of domestic animals having been largely due to the bites of foxes, among which the disease was extremely prevalent. The epidemic affected at least one-half of the island territory and losses among livestock were heavy. Diagnosis was established by histological examination and experimental animal inoculation of material recovered from domestic animals dead of the disease. The virus is stated to have been identical with the North African strain. Although the epidemic was confined to the animal population, 167 persons presented themselves for anti-rabies treatment—121 at the emergency treatment centre established at Ajaccio where phenolized vaccine was employed and 46 at continental Pasteur Institutes. No case of human rabies was reported, no ill effects of treatment occurred.

Measures of control included : prophylactic vaccination of dogs and herbivorous animals ; the restricted movement of dogs ; and the destruction of foxes by shooting, trapping or poisoned bait. Doubt is expressed as to whether the infection has actually been extinguished.

[An epizootic among foxes has troubled the South-Eastern States of the U.S.A. for some years.] *G. Stuart*

BÉQUIGNON, R. ; LAMY, R. ; VIALAT, C. ; BUSSARD, A. Contribution à l'étude de la rage. I. De la virulence de la rage fixe par voie sous-cutanée après addition de bave de chien normal [BÉQUIGNON, LAMY & VIALAT]. [**Contribution to the Study of Rabies. I. On the Virulence of Fixed Virus administered subcutaneously after the Addition of Healthy Dog's Saliva.**] *Ann. Inst. Pasteur.* 1949, Mar., v. 76, No. 3, 283–5. II. De la virulence de la rage fixe par voie sous-cutanée après addition de hyaluronidase [BÉQUIGNON, BUSSARD & VIALAT]. [**On the Virulence of Fixed Virus administered subcutaneously after the Addition of Hyalurodinase.**] *Ibid.* 285–6.

In the first of the articles under review the authors describe an experiment carried out with a view to determining whether or not the rôle played by the

saliva of a biting animal is purely a mechanical one. For the experiment, saliva was obtained from a healthy dog previously injected with pilocarpine and the fixed virus from the PASTEUR strain at its 1809th passage—a strain which had long lost its power of transmission by the subcutaneous route. To an emulsion of 1 : 10 by weight of this fixed virus was added an equal volume of saliva, the mixture being placed in the incubator for 1 hour at 22°C.

To each of 4 guineapigs 1 cc. of the mixture was administered subcutaneously in the flank on 1st December 1948 and on the same date each of 4 control guineapigs received in the same region 1 cc. of the mixture which, in this case, had not been kept in the incubator.

Of the first group, one developed typical paralysis on 9th December and was sacrificed, when at the point of death, on the 16th December. A second became paralysed on the 15th December and was sacrificed on the following day. The third and fourth animals escaped infection. Of the second group, none was affected. What factor was responsible for the alteration in behaviour of the fixed virus ? In the authors' opinion it was an enzyme, not amylase (as proved by previous investigation), but probably hyaluronidase, their belief being based on the findings of DURAN REYNALS (*C. R. Soc. Biol.*, 1928, v. 99, 6) and of HOFFMAN (*J. Exper. Med.*, 1931, v. 53, 43), who had some 20 years ago demonstrated the influence of that enzyme as a " spreading factor " on a number of viruses.

In the second article the authors describe how, using hyaluronidase obtained from testicular extract of the bull, they were able to effect a change in the behaviour of the fixed virus when injected subcutaneously into guineapigs identical to that obtained with the saliva of a healthy dog. Thus the belief expressed in their first article received strong support.

It is of interest to note that, in the guineapigs sacrificed in the first series of experiments, histological examination of the neural axis showed not only lesions typical of fixed virus rabies but also, at the level of the neurones in the outer layer of Ammon's horn, nuclear lesions of a type unknown to the authors. There was frequent occurrence, in the same nucleus, of 2 nucleoli in every way comparable, but most marked was the presence, in nuclei still retaining their normal arrangement of chromatin, of oxyphilic bodies, like the nucleoli, varying in dimension up to the size of nucleoli and attached thereto in twos and threes. Such bodies, arranged symmetrically when small, tended to take up a position further from the nucleolus in proportion to their increase in size and to approach the inner coat of the nuclear membrane, a clear halo surrounding those of larger size. None of these formations was observed in the cytoplasm of the neurones. Similar findings were encountered in the second series of experiments.

G. Stuart

LIEOU, Y. C. **Carriers of Rabies Virus.** *Chinese Med. J.* 1948, Dec., v. 66, No. 12, 694–9. [33 refs.]

The author defines a carrier of rabies virus as " one who, with all the external signs of good health bears, nevertheless, in his organism a virus, detectable either by experimental inoculation or by microscopical examination ". He divides carriers into four categories, according to localization of virus, *viz.*, in the brain, blood, saliva and subcutaneous tissues. The following paragraphs summarize his presentation of the subject :—

Virus carried in the brain.—Experimentally virus, after intracerebral inoculation, may lie latent, unaltered and without causing symptoms, for long periods (90–302 days respectively) in the brain of the fresh water turtle

and land tortoise—cold-blooded animals refractory to rabies—and for shorter periods, up to 23 days, in pigeons—warm-blooded and relatively insusceptible to rabies [probably because of their high body temperature] (phenomenon of permanence). In dogs, inoculated subdurally, the virus may disappear from the brain for several days and then reappear (eclipse phenomenon). Under natural conditions the virus may remain dormant, for months, even years, in the brain of man, especially in the inadequately treated until suddenly awakened to action by stimuli such as trauma, cold or emotional upset.

Virus carried in the blood.—Experimentally the presence of virus in the blood of rabbits, 4–5 days after subdural inoculation, has been demonstrated by MARIE & URBAIN [this *Bulletin*, 1931, v. 28, 746]. The present author also has shown that rabbits inoculated intraperitoneally may early contain virus in their blood and remain unaffected throughout a four months' period of observation. In nature, as stated by REMLINGER and by KONRADI, a female animal can transmit rabies to its offspring by way of the placental circulation. [These findings and observations are not generally accepted. Many workers on rabies consider that the blood is non-infectious in man and in experimental animals and that virus cannot be conveyed to the foetus. Other workers believe that, after experimental inoculation, the blood rarely proves infectious, *i.e.*, rarely contains virus ; in positive findings the appearance of virus is but momentary.]

Virus in the saliva.—Animals generally transmit rabies by their saliva ; this group of carriers is, therefore, most important from a practical point of view. A dog in the incubation period of the disease may, when apparently healthy, convey rabies by its bite, inasmuch as it may have virus in its salivary glands as early as 10–11 days before showing first symptoms. [How long virus is present in the saliva before the animal becomes outwardly ill is not established, but it is probably 2–5 days.] Recovery from rabies is relatively frequent in adult birds. Should a dog recover, it remains a carrier of virus. [According to REMLINGER the saliva of a dog remains virulent five days after recovery. Most workers, who have studied experimental rabies in dogs, have noted apparent recovery from paralytic disease. There is no record, however, of isolation of rabies virus from the saliva of a naturally infected dog that eventually recovered. Moreover, with the possible exception of the dog reported by REMLINGER (1907), it has been impossible to isolate virus from the saliva of experimentally infected dogs that did not succumb. It should be noted that REMLINGER's findings were in respect of a dog which had been inoculated with fixed virus and that other investigators have failed to isolate virus from the salivary glands of dogs infected with fixed virus.]

Virus carried subcutaneously.—All individuals, who receive anti-rabies vaccine prepared according to the method of PASTEUR, HOEGYES or FERMI, must at some time during the course of treatment harbour virus subcutaneously. In dogs immunized with wholly inactivated vaccine, rabies virus, on later introduction by a biting animal, rapidly disappears ; such immunized dogs do not, therefore, become virus carriers. [Unlike all other known vectors, which transmit the disease for a limited period of time and then die of the infection, the vampire bat is capable of transmitting rabies over periods of 6 months as a symptomless carrier. These bats are " carriers ", in that they are infected with the virus and transmit it to others by biting—their saliva is infected—and yet are sufficiently resistant to hold it in check in their tissues without developing the disease and succumbing to it. In rabies, then, as in other infections, there exist healthy carriers of the virus which are capable of transmitting the virus and, consequently, the disease.] *G. Stuart*

[A number of the references in this paper are inadequately cited.—*Ed.*]

Jonnesco, D. Rage chez l'homme par morsure de rat. Virus renforcé. [**Rabies in Man following Rat Bite. Virus of Hypernormal Virulence.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1945–1946–1947, v. 14, Nos. 1/4, 186–8.

The fact that no previous case of human rabies following rat-bite would appear to have been recorded and that the present occurrence might suggest the need for amplifying existing measures of control over the animal reservoirs of rabies occasioned the writing of the article under review. On 15th December 1945 a male, aged 29 years, was bitten deeply on the palmar surface of the right thumb by a rat which immediately disappeared. On 16th January 1946 the patient, who had neither applied for nor received anti-rabies treatment, developed symptoms characteristic of hydrophobia and died 3 days thereafter. Portions of the brain of the deceased were investigated by histological examination and by animal inoculation. Histological examination revealed the presence of lesions similar to those found in other encephalitides, but an absence of Negri bodies in Ammon's horn and elsewhere.

As regards animal inoculation : subdural inoculation of rabbits with 0·2 cc. of a 1 : 200 brain emulsion evoked symptoms in 3 days—an incubation period which remained fixed in respect of further rabbit series inoculated. Similarly the original incubation periods of 2 days and 4 days, following respectively the intracerebral inoculation of guineapigs and dogs, remained constant in subsequent passages. Moreover, of 10 white mice inoculated subcutaneously with 0·5 cc. of a 1 : 200 emulsion, 7 became paralysed in 5 days and 3 after 6 days.

It is held, therefore, that this particular virus which, transferred by rat-bite, produced rabies in man after an incubation period of 32 days, can be classified as a virus of hypernormal virulence (*renforcé*), in view of the fact that from all passage series Negri bodies continued to be absent and that, as from its first passage, the incubation period in rabbits, guineapigs and dogs remained fixed at 3, 2 and 4 days respectively ; further, on subcutaneous inoculation, the virus was pathogenic for white mice in every case. *G. Stuart*

Jonnesco, D. & Olaru, Cornelia. Considerations sur l'action du traitement antirabique sur le fonctionnement ovarien. [**Observations on the Effect of Anti-Rabies Treatment on Ovarian Function.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1945–1946–1947, v. 14, Nos. 1/4, 189–92.

Impressed by an increase in the menstrual disorders of certain women to whom courses of anti-rabies vaccine had been administered, the authors sought by experimental research and clinical observation to discover the probable cause of such disorders. Experimental research was directed towards the establishment of a possible connexion between the disorders and the quantities of ovarian hormones secreted respectively before the beginning of treatment and 30 days after its completion. To this end estimations of the amounts of prolan and of folliculin eliminated in the urine of 8 women, aged from 18 to 31 years, were made before and after treatment. Before treatment, 1 subject eliminated 20 mouse-units of prolan per litre, 3 cases 12 mouse-units and 5 cases less than 5. All 8 subjects eliminated less than 10 mouse-units of folliculin per litre. After anti-rabic treatment, 1 subject eliminated 50 mouse-units of prolan per litre, 5 eliminated 20 and 2 eliminated 12 mouse-units. Two subjects eliminated 10 mouse-units of folliculin and 6 less than 10. Thus anti-rabies vaccination effects a hypersecretion of prolan and folliculin, as compared with the normal secretion of these hormones prior to treatment.

Clinical observations made on 12 women, of from 15 to 48 years of age, revealed a continuous stimulation of the ovary both during and after anti-rabies treatment—a stimulation evidenced by marked irregularity of menstruation. It was found that the more the treatment was prolonged, the greater was the degree of disturbance ; thus one woman treated over a period of 25 days twice experienced the menstrual flow during that time. The authors conclude, therefore, that anti-rabies treatment produces a disturbance of ovarian function. *G. Stuart*

ROANTREE, W. B. **Surgical Treatment of Rabies.** [Memoranda.] *Brit. Med. J.* 1949, May 21, 900.

Complete destruction of rabies virus in wounds by cauterization alone is at best fortuitous and unlikely to occur in extensive, deep or punctured wounds. The author, writing from Kolar Gold Field, India, quotes three fatal cases, in two of which cauterization had been employed ; but he admits that the risk of rabies had been great. The patients had also had full, but somewhat delayed courses of anti-rabic vaccine.

He suggests that cauterization might well be combined with the modern surgical technique of excision of contaminated wounds : he briefly outlines such a treatment which consists principally of the following steps :

(1) Thorough cauterization immediately with concentrated nitric or pure carbolic acid.

(2) Careful sterilization of the skin over a wide area with pure rectified spirit and then with tincture of iodine.

(3) Surgical excision *en bloc* of all lacerated and potentially infected tissue. Dissection should be made in uncontaminated tissue planes, with an ample barrier of clear tissue. A fresh knife is necessary for each wound, contaminated instruments should be kept rigidly separate and treated with lysol, washed and sterilized at the earliest moment.

(4) The surgical wound is cauterized with the original cauterizing agent. After haemostasis is secured, it is left unsutured and dressed.

Dr. N. Veeraraghavan, Director of the Pasteur Institute, Coonoor, pointed out to the author that in experimental animals, rabies occurs as quickly by inoculation of the sciatic nerve as of the subdural space : He raised the question of such inoculation of nerve trunks during surgical excision of the wound : the present author believes it to be likely that this could be avoided by immediate cauterization and careful avoidance of operative contamination.

He suggests that there is ground for testing this procedure experimentally. If it proved effective, the method would be indicated in cases where (1) strong presumptive evidence of rabies infection was present, (2) wounds were amenable to radical excision, (3) adequate surgical facilities were available.

In more remote areas, cauterization alone would of course be necessary for local treatment : and in any case a full course of anti-rabic vaccine would be required. *H. J. O'D. Burke-Gaffney*

WRIGHT, J. T., BELL, J. F. & HABEL, K. **Benzene-Ether Extracted Rabies Vaccine.** *Science.* 1948, July 30, 118–19.

Believing that their previous efforts at sharp separation of the rabies virus from tissue elements had been largely frustrated by the presence of brain lipoids, the authors, as an initial step in the purification of rabies vaccine, attempted the preparation of vaccines by extracting these lipoids with various solvents (acetone, benzene, carbon tetrachloride, dichlorethylene). The technique followed may be thus summarized : To the homogenized, infected,

brain tissue dried from a frozen state under vacuum the lipoid solvents were added, the volumes in each case being about twice the wet volume of the original tissue suspension. After 2 hours in the cold room, the solvent was removed by centrifuging and decanting or by filtration ; in either case the residue was resuspended in the solvent and at once recentrifuged or refiltered. Thereafter, with ether at –50°C., extraction was carried out in a similar way. The tissue was then freed from any residual ether by placing the container in a jar and exhausting by water suction.

Inasmuch as benzene extraction was found to provide the most potent antigen and proved to be least toxic to the rabies virus, further experimentation was undertaken, with the use of that solvent for extraction. Results of such experimentation went to show : (1) Extraction with cold benzene and ether does not inactivate all the rabies virus in brain tissue but causes a marked reduction in the infective titre ; (2) rabies vaccines, killed by preliminary ultraviolet irradiation and then extracted with benzene, suffer no loss of antigenicity ; indeed they show, in most cases, a heightened antigenicity ; and (3) rabies vaccines extracted according to the cold-benzene-ether method described above had much of their lipoid content (41·5 per cent. of the total dry weight) removed, thus eliminating " one of the major non-specific components of a very crude vaccine."

As a result of their experiments the authors conclude that, for the prevention of rabies, benzene and ether-extracted vaccines may offer some advantage over unextracted vaccine. *G. Stuart*

Habel, K., Bell, J. F. & Wright, J. T. **Benzene-Inactivated Rabies Vaccine.** *Proc. Soc. Exper. Biol. & Med.* 1949, Mar., v. 70, No. 3, 455–7.

In a previous article the authors [above] detailed a technique for the extraction, by benzene and ether, of infected, dry brain tissue containing rabies virus inactivated by ultraviolet light. Irradiation had then been employed for inactivation, because it was known to yield vaccines of high antigenic potency and because cold benzene and ether did not inactivate all of the virus.

In the present paper the authors describe a method for the inactivation of rabies virus by benzene alone during the course of extraction of brain tissue lipoids with that solvent. From experimental work it emerged that the virus contained in anti-rabies vaccines prepared from mouse and rabbit brain tissue could be wholly inactivated by exposure to benzene at 56°C. for 12 hours and that the vaccines so treated showed no decrease in antigenic potency. Moreover, tests on mice and rabbits to determine the comparative antigenicity of benzene-inactivated and ultraviolet light-inactivated vaccines afforded proof that, when there were differences, the benzene-inactivated vaccine in most instances showed the higher potency. From the above findings it may be concluded that inactivation of rabies virus by heating in benzene results in a highly potent vaccine and that the need for preliminary ultraviolet irradiation has been eliminated. *G. Stuart*

Bell, J. F., Wright, J. T. & Habel, K. **Rabies Vaccine freed of the Factor causing Allergic Encephalitis.** *Proc. Soc. Exper. Biol. & Med.* 1949, Mar., v. 70, No. 3, 457–61.

The neuroparalytic accidents of anti-rabies treatment—post-vaccinal encephalomyelitis in man and its apparent counterpart, experimental allergic encephalitis in lower animals—are conditions which may occur when brain

tissue is injected parenterally. The aetiological agent concerned in the production of these accidents has long been sought and now, as a result of the authors' successful search for an anti-rabies vaccine containing antigens of high potency, yet freed of the factor which causes allergic encephalitis in animals, the solution of the problem has been brought appreciably nearer. Such a vaccine was thought already to have been discovered when the authors, at an earlier stage of their investigations, had managed to remove the lipoids from the virus by treating the rabies-infected brain tissue with benzene and ether ; for at that time they believed that the removal of the lipoid components might also eliminate the material responsible for the paralysis. Experience showed, however, that their benzene-ether-extracted vaccine, while suffering no reduction in antigenicity, still retained its capability of producing paralysis in guineapigs.

In their efforts to remove from anti-rabies vaccine this paralysis-producing factor, the authors had recourse to further experimentation, during the course of which it emerged that, after washing with M/10 calcium acetate solution followed by distilled water, the virus antigen was precipitated from the vaccine without loss of its antigenic potency and such precipitate remained insoluble in water ; the residual washed vaccine contained but 50 per cent. of the total nitrogen of the original vaccine and had a calcium content of 0·005 per cent. ; the factor causing allergic encephalomyelitis was present in the calcium acetate solution removed by filtration and could no longer be demonstrated in vaccines which had been previously treated with benzene and ether. Vaccines not previously so extracted were not freed of the factor causing paralysis when similarly washed with calcium acetate.

In view of the very great importance of the work described in the paper under review and of the possibilities which the findings hold out for the later employment in man of a wholly safe anti-rabies vaccine of high potency, it is considered desirable to quote the authors' summary of their paper :—

" A method has been presented for the removal from rabies vaccine of the factor which causes allergic encephalomyelitis. This factor is not removed by extraction with benzene and ether, but preliminary treatment of the vaccine with these solvents facilitate separation by subsequent treatment. The presence of calcium acetate prevents the loss of antigen when the vaccine is washed. It does not prevent removal of the encephalitic factor which appears to be water soluble. About one-half of the total nitrogen of the vaccine is removed by this washing process.

" The technic may be briefly summarized as follows :—

" (1) A suspension of infected brain in water is dried from the frozen state.

" (2) The dried brain is extracted with benzene followed by ether (live virus may be killed in this stage by heating in benzene).

" (3) After removal of the ether the dried brain is suspended in distilled water.

" (4) Sufficient solution of calcium acetate is added to make final concentration of M/10 calcium acetate, and the suspension is permitted to stand in the cold for an hour or two.

" (5) The calcium acetate solution is removed by centrifugation or filtration and the sediment is resuspended in distilled water to the original volume with agitation (clumps of sediment must be broken up).

" (6) The distilled water is removed by centrifugation or filtration.

" (7) The sediment is resuspended in distilled water or saline and homogenized. This is the washed vaccine." *G. Stuart*

KOPROWSKI, H. **Experimental Studies on Rabies Virus.** *Canadian J. Pub. Health.* 1949, Feb., v. 40, No. 2, 60–67.

It is agreed that one of the most effective measures of rabies control is the mass prophylactic vaccination of dogs but, militating against the successful application of such measures have been, in particular, the necessity for multiple vaccinations and the recorded occurrence of post-vaccinal neuroparalytic accidents. The studies described in the article under review were undertaken primarily with a view to discovering an efficient " single injection " method of canine immunization which, in practice, would be free from the risk of subsequent paralytic accident.

That the egg-adapted FLURY strain of rabies virus gave greatest promise for the development of a vaccine which would meet these requirements was confirmed and extended by the author's experimental work. Thus guineapigs inoculated extraneurally, although slightly susceptible to the low egg-passage levels of the strain, became almost completely refractory to the higher level passages, and only occasionally did one animal out of ten inoculated with 20 per cent. suspension of infected embryos show any signs of paralysis. Conversely, the immunity response of the surviving guineapigs, later challenged with street virus, was highly satisfactory.

Further, repeated experiments adduced abundant proof that the FLURY strain given parenterally is innocuous for the canine species. Thus dogs, which received the intramasseter inoculation of a 20 per cent. embryo suspension, survived the 12 months' observation period without having shown any sign of illness. Similarly animals which had been inoculated in the muscles of the hind legs with 5 cc. of a 20 per cent. suspension of the virus, or by the intramasseter route with a 40 per cent. embryo suspension remained without ill-effect during the entire periods of their observation (2 to 6 months).

Encouraged by these results, the author then attempted a determination of the immunizing power of the FLURY strain in dogs. Animals were vaccinated in the muscles of the hind legs with a single 5 cc. injection of either fresh or lyophilized preparations consisting of either a 20 per cent. or 40 per cent. suspension of infected chick embryos at various egg-passage levels and then challenged, at different intervals, varying from 5 to 27 weeks, by bilateral intramasseter inoculation with a 10 per cent. suspension of street virus giving mouse-intracerebral LD 50 titres of $10^{-4.50}$ to $10^{-6.15}$. Of 66 dogs vaccinated, only 2 succumbed to the massive test inoculation, whereas 23 of the 37 control dogs died. Duration of such immunity in dogs is now under study.

Turning to the protection of human beings against rabies and the development of a procedure which would be as effective as the PASTEUR treatment but would not carry with it the danger of neuroparalytic accident, the author suggests the substitution of anti-rabies serum for the vaccines now in use. Experiments on the protective power of the serum (a concentrate of the beta- and gamma-globulin-containing fractions of pooled rabbit plasma fractionated by sodium sulphate precipitation) were carried out on hamsters along lines corresponding to those encountered in nature, *i.e.* first infection with street virus, followed by treatment ; the remarkable protective value of one injection of antiserum, as contrasted with the lack of value even after full courses of phenolized vaccines in massive dosage or of living virus vaccines, was clearly demonstrated. Factors found to influence the action of the serum included its degree of dilution, the amount of virus present in the infecting inoculum and the time-interval between infection and treatment.

In the author's opinion, " the general evidence in favour of serum treatment is so conclusive, especially as the danger of neuroparalytic accidents following

serum treatment does not exist, that a thorough field trial of serum prophylaxis in rabies is fully warranted." *G. Stuart*

Béquignon, J. R. & Vialat, C. Les vaccinations antirabiques à l'Institut Pasteur en 1947. [**Anti-Rabies Vaccinations at the Pasteur Institute in 1947.**] *Ann. Inst. Pasteur.* 1948, Aug., v. 75, No. 2, 163–7.

This Report details the procedure followed at the Pasteur Institute of Paris in the treatment of persons exposed to the risk of rabies infection and provides statistics for the year 1947. During that year 212 bitten persons received treatment ; no rabies death occurred ; and no neuroparalytic accident followed treatment. Animals incriminated in the biting of the persons treated were 175 dogs, 28 cats and 9 rats ; these animals included 1 in category A (proved rabid experimentally), 3 in category B (diagnosed rabid clinically) and 208 in category C (suspect only). It is noted that 1947 was the 23rd successive year in which no rabies death occurred among persons treated at the Institute.

Of the 54,990 persons treated during the 62 years' period 1886–1947, there were 7,083 bitten by animals in category A, 27,190 by animals in category B and 20,717 by animals in category C ; 151 died of rabies, thus providing a percentage mortality of 0·28. *G. Stuart*

PLAGUE

Bernard, L., Dounet, G. & Jaujou. Une épidémie de peste bubonique à Ajaccio (1945). [**An Epidemic of Bubonic Plague at Ajaccio (1945).**] *Rec. Travaux Inst. Nat. Hyg.* Paris. 1948, v. 2, 355–75, 2 figs.

In this outbreak 13 persons were attacked within a period of 10 weeks in the months May, June, and July, 1945. The disease had not been known to occur in the Island of Corsica within living memory, so the infection must have been introduced by the sea route.

Reference is made to the finding of dead rats before the outbreak, but these were not examined. All the 148 rats trapped afterwards were found free from infection ; of these 14 were *Rattus rattus alexandrinus* and the rest were *R. norvegicus*. On the 148 rats only 101 fleas were found ; 42 of these were *Xenopsylla cheopis*, of which all but 8 were found on the 14 specimens of *R. rattus*.

The outbreak was confined to three small areas, one of which was a military barrack. All the usual measures of control were very thoroughly carried out, including the compulsory vaccination of all the 25,000 inhabitants of Ajaccio. The complete disappearance of the disease was attributed partly to the scarcity of the vector fleas and partly to the measures of control that were adopted.

John W. D. Megaw

Tchan, Y. T. Culture de *Pasteurella pestis* à partir d'un seul microorganisme. [**Cultivation of** *Pasteurella pestis*, **starting from a Single Cell.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 3/4, 89–91.

Using a micromanipulator the author has succeeded in isolating single cells of *P. pestis* on ten occasions from a suspension of the organisms maintained in peptone water for four hours at a temperature of 34°C. In three cases a single cell gave rise to cultures on peptone agar. For details of the technique the original paper must be consulted.

The cultures have been made over to G. Girard who proposes to study them from the point of view of obtaining living attenuated vaccines originating from single cells; the original culture used by the author was of an avirulent strain.

John W. D. Megaw

DEVIGNAT, R. La prophylaxie de la peste au Lac Albert par l'association de la dératisation et de la vaccination (virus-vaccin E. V. de Girard et Robic). [**Plague Prevention in the Lake Albert Region by Rat Destruction combined with Vaccination with the Girard-Robic Vaccine.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 1/2, 43–52, 1 graph.

This paper deals with plague prevention as practised during the years 1937–46 in a zone of 100 by 40 kilometres on the west shore of Lake Albert on the borders of the Belgian Congo.

Every month a gang of rat catchers visits each occupied hut in the zone and seeks out the nests of the rats. The result has been an apparent increase in the rat population, the average number found in each hut was less than one in 1937–38 and it now ranges from 2·1 to 2·5. The average number of fleas found on each rat has, however, been considerably reduced—to about one-third of the previous figure.

During 1939 and 1940 the rat-flea population was at its lowest, yet these were the years of highest prevalence of plague.

The rat-catching campaign was maintained as a means of detecting the presence of infection; pooled suspensions of femoral bone marrow of all the rats caught in each village were inoculated into guineapigs and when infection was detected the villagers were inoculated with the Girard-Robic living avirulent vaccine. [See this *Bulletin*, 1939, v. 36, 314.]

During the whole period about 400,000 doses of vaccine were given, and the author is satisfied that it was highly effective; there were only 16 cases of plague among the vaccinated against 116 among [an unstated number of] unvaccinated persons. The earliest attack in a vaccinated person occurred three months after vaccination.

An increase in virulence of the living vaccine occurred on one occasion, but the virulence was reduced to the former low level by passing a stream of air through a solution of caustic potash and then through broth cultures of the strain. This process was continued for eight days; it had already been found effective in reducing the virulence of three local strains of fully virulent *P. pestis*.

John W. D. Megaw

DAVIS, D. H. S. **Current Methods of controlling Rodents and Fleas in the Campaign against Bubonic Plague and Murine Typhus.** *J. Roy. San. Inst.* 1949, May, v. 69, No. 3, 170–75.

A useful survey of present methods.

GRATCH, I., PURLIA, P. L. & MARTIN, M. L. **Effect of Sodium Fluoroacetate (1080) in Poisoned Rats on Plague Diagnosis Procedures. Preliminary Report.** *Pub. Health Rep.* Wash. 1949, Mar. 18, v. 64, No. 11, 339–42.

By fully controlled experiments the authors have found that rats poisoned with sodium fluoroacetate are just as suitable for bacteriological examination to detect the presence of plague infection as are rats caught by trapping or poisoned by hydrocyanic acid gas.

As ordinarily used the fluoroacetate does not reach the liver of the rat in quantity sufficient to damage guineapigs inoculated with suspensions of the

liver, and it has no adverse effect on the viability of *Pasteurella pestis* contained in the tissues of infected guineapigs.

In vitro the poison was found remarkably free from bacteriostatic effect on cultures of *P. pestis*. *John W. D. Megaw*

SERGENT, Ed. & SERGENT, Et. Nouveau procédé de dératisation basé sur l'emploi du D.D.T. [**A New Method of Rat Destruction by DDT.**] *Arch. Inst. Pasteur d'Algérie*. 1949, Mar., v. 27, No. 1, 18–30, 1 fig. [Refs. in footnotes.]

A powder, containing 50 per cent. DDT, deposited in and round the entrances of rat holes has been found to kill within a few days about 80 per cent. of the rats. The powder is left permanently to ensure cumulative action of the poison.

No details of the quantity applied are given except for the statement that the powder is used in the same way as for the destruction of cockroaches. For mice a 5·0 per cent. powder is said to be effective.

Although the powder is not highly toxic for man and domestic animals precautions are recommended against the risk of contamination of foodstuffs and of contact with domestic animals, especially cats.

John W. D. Megaw

CHOLERA

DE MOOR, C. E. **Paracholera (El Tor) : Enteritis Choleriformis El Tor van Loghem.** *Bull. World Health Organization*. Geneva. 1949, Mar., v. 2, No. 1, 5–17, 2 maps. [Refs. in footnotes.]

Following on earlier reports on choleriform disease in Celebes attributed to a haemolytic vibrio [this *Bulletin*, 1939, v. 36, 374] another account of investigations on the subject is given with a discussion of its epidemiological significance. The questions are raised (1) whether the haemolytic vibrio of Celebes and *Vibrio El Tor* are identical, (2) whether the disease in the Celebes is distinguishable from cholera, and (3) whether quarantine regulations should be applied against cases and carriers from which the El Tor type of vibrio is isolated.

The Celebes cases were not distinguishable clinically from Asiatic cholera and the mortality varied from 69 to 75 per cent.

Bacteriology.—Strains of the haemolytic vibrio were examined which had been isolated from 370 sources in the Celebes including patients, contacts, and other healthy persons and from wells both in the vicinity of cases and in areas where the choleraic condition had not occurred. All strains were serologically identical with *V. cholerae* and the El Tor vibrio by the usual agglutination tests with cholera O-serum, the majority being of the Ogawa type and the remainder of Hikojima type. They could however be differentiated from *V. cholerae* by special tests. When a thick suspension of the haemolytic vibrio in distilled water was added to a 1 in 200 dilution of cholera O-serum in 0·3 per cent. Na_2CO_3. H_2O it promptly agglutinated : a suspension of *V. cholerae* similarly treated remained unaffected. A thick suspension of *V. cholerae* in 0·5 per cent. $NaHCO_3$ was completely precipitated when mixed with an equal volume of a 0·5 per cent. solution of $HgCl_2$, but a suspension of the El Tor vibrio remained stable.

A study of the haemolytic action of the Celebes and El Tor vibrios showed the following to be characteristics of newly isolated strains ; (1) haemolysis in blood broth within 24 hours growth, (2) positive Greig test with broth culture and (3) beta-haemolysis on anaerobically incubated blood agar. Greig's test

was usually positive with broth cultures 12-hours old, the haemolysis being strongest with cultures 2-days old, but cultures 4-days old were no longer haemolytic. In the refrigerator a broth culture retained its haemolytic power for weeks. Cholera strains were found to show only slight haemolysis in blood broth cultures and at the earliest after 48 hours growth : Greig's test was always negative. On blood-agar, only digestion of blood-pigment was visible.

The test for acetylmethylcarbinol by Barritt's method was not fully differential.

No difference in behaviour was demonstrated between the vibrio of Celebes and that of El Tor.

The epidemics. The first outbreak described consisted of 48 cases distributed over a period of eight months from September, 1937, to April, 1938, with a very scattered distribution. The second series occurred between October, 1939, and April, 1940, and included 37 cases within a radius of 20 km. around Lake Tempe and 26 cases divided between two areas of the East Coast. The third series consisted of 7 cases in 1946 which were also widely scattered. The total recorded from September, 1937 to December, 1944, was 118 cases in 70 *kampongs*. There was no seasonal incidence, cases occurring both in an extremely dry season and in a wet season of the year. Cases were sporadic and there was no tendency to spread to large centres of population in spite of extensive road traffic. In view of the very low and scattered incidence and the absence of epidemic tendency the mass inoculation and isolation measures which were at first applied were later omitted.

Incidence of the vibrio. The vibrio was isolated from the stools of 10 per cent. of 579 family contacts examined, and from 42 per cent. of the 132 wells used by patients. Half of the family contacts examined continued to excrete the vibrio after one week but, with one exception, they became permanently negative after 11 days : the vibrio was recovered intermittently from the exceptional case up to 27 days. The examination of 5,566 healthy persons in the infected area who were not family contacts resulted in the vibrio being isolated from 21 (0·4 per cent.). The organism was also isolated from 43 out of 1,023 wells (4 per cent.) in *kampongs* in these areas. In *kampongs* where cases had actually occurred it was isolated from 0·9 per cent. of 1,225 healthy persons and 6 per cent. of 172 wells. In uninfected areas, and even where the disease had never been noted, the vibrio was occasionally found.

Epidemiological considerations. The opinion is expressed that the El Tor vibrio is an accidental resident in water but does not thrive there. The author considers infection of wells and rivers with the El Tor vibrio to be of human origin and that the vibrio is maintained by successive groups of persons becoming temporary carriers ; chronic carriers are not found. Vibrios in wells act as indicators of human infection.

The sporadic and static character and the low mortality of the disease attributed to the El Tor vibrio are in striking contrast with the epidemic nature of cholera with its tendency to spread and its high morbidity. After an epidemic the cholera vibrio disappears from the community while the El Tor vibrio may remain in an area for prolonged periods and may even be found where no cases of choleriform disease have occurred.

" Occasional pathogenicity, static character, sporadic occurrence, and slight morbidity explain why the El Tor disease has not been encountered during the Mecca pilgrimage and in countries around the Red Sea (Hejaz, Egypt and Iraq) and in Bengal and Madras where the true El Tor vibrio has been found in healthy persons or in wells."

The El Tor disease is a commensal infection and is sporadically of endemic nature while cholera is a parasitic infection and is endemic. It is suggested the disease caused by the El Tor vibrio should be designated "paracholera El Tor".

" Quarantine, strict isolation of sick persons, disinfection and mass immunization are not justified in the case of paracholera because this disease does not spread epidemically and claims in the long run few victims. However, so long as there is no general agreement on the identification of the El Tor vibrio, a paragraph will be necessary in any international quarantine convention on cholera, regulating the official notification of cases of paracholera (El Tor) and of carriers of the El Tor vibrio." Van Loghem is quoted as stating that " If the difference in kind between *Vibrio cholerae* and *Vibrio El Tor* is recognized there is no question of cholera asiatica but of an El Tor disease." He proposed the term " enteritis choleriformis El Tor."

[The observations presented support the usual practice of not applying quarantine measures when the El Tor vibrio is isolated. It can readily be differentiated from *V. cholerae* to which alone quarantine regulations will apply and it would hardly be necessary to make special regulations in regard to it.]

J. Taylor

VEERARAGHAVAN, N. **A Simple Medium for Cultivation of *V. cholerae*.** [Correspondence.] *Nature.* 1949, Jan. 22, 138.

Heavy growth of *V. cholerae* was obtained in a liquid medium consisting of a salt mixture with *l*-cystine, glucose and " Marmite " at initial *p*H of 8·8, when alkalinity was maintained by the periodical addition of sodium bicarbonate and small quantities of glucose added at the same time. Ammonium sulphate was included in the salt mixture and without it growth ceased at the end of 10 hours. When sodium bicarbonate and glucose were added at 10, 16 and 24 hours from the beginning of incubation and the *p*H raised to the vicinity of 8·0 the concentration of vibrios in the culture reached 12,000 to 14,000 million at the end of 30 hours.

J. Taylor

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

COELHO, E. **Rectal Swab in the Investigation of Diarrhoeas in Children.** *Indian J. Med. Sci.* 1949, Apr., v. 3, No. 4, 266–71.

The apparatus required for preparation of rectal swabs consists of a proctoscope, glass slides and cover slips, normal saline, iodine solution, soft paraffin and " broom sticks " to which the cotton swabs are attached. The results of examination of rectal swabs in 229 acute and 74 chronic cases of diarrhoea demonstrate that the rectal swab provides a sample of the rectal contents adequate to discover all the abnormal findings normally found on faeces examination.

A second table, in a comparison between rectal swab and stool examination in 59 patients, shows that " a percentage of acute diarrhoeas in children is due to a bacillary infection." The figures for macrophage cells are nearly equal while for pus cells the sample from the rectal swab is definitely better; moreover it gives a positive result for *E. histolytica* more often, particularly for the active trophozoites, and it is also better for the detection of *Giardia intestinalis*. A search through voided stools is more profitable for finding round worm ova. In " normal " patients the rectal swab detected more with *Giardia* and cysts of *E. histolytica*. In 15 out of 30 patients the rectal swabs failed to reveal anything but there were only eight negative results with stool examination.

The rôle of giardiasis in acute and chronic diarrhoeas of children is important. Out of 310 acute diarrhoeas 16·4 per cent. were due to this infection, as were 43 per cent. of 130 chronic diarrhoeas. The youngest child in whom *Giardia* was found was 14 days old. *P. Manson-Bahr*

REDDY, D. G. & THANGAVELU, M. **Some Aspects of Amoebiasis in Madras.** *Indian Med. Gaz.* 1948, Dec., v. 83, No. 12, 557–63, 6 figs. on 2 pls. [25 refs.]

An analysis of 2,641 cases treated in the General Hospital, Madras, is as follows :—

Dysentery	Total number of cases	Percentage of incidence	Number of deaths	Percentage of deaths
Amoebic	1,011	38·3	62	6·13
Bacillary...	1,345	50·9	134	9·9
Mixed	28	1·1	1	3·8
Non-specific	257	9·7	37	14·4

In children the incidence of amoebic infection is low. This is well brought out by figures shown in a table. Males are infected more frequently than females. Amoebiasis in general does not exhibit that seasonal incidence which is so characteristic of bacillary dysentery. In 44 postmortem examinations intestinal lesions were found in 38 and hepatic lesions only were seen in the remaining six. In most cases, the primary lesion began in the caecal area, but with the progress of the disease the entire colon seems to become involved. In only two cases was amoebic involvement of the appendix observed, but the rectum is frequently affected. Amoebic granuloma was occasionally seen. An account of six such cases has already been published [this *Bulletin*, 1947, v. 44, 583.] Amoebic ulceration may co-exist with typhoid.

From 1941 to 1946 1,534 cases of hepatitis were treated in the Government Hospital, Madras, and of these 364 (30 per cent.) were diagnosed as being of amoebic origin ; during the same period 84 cases of liver abscess were treated in the surgical wards of the General Hospital and 40 in the King George Hospital, Vizagapatam. The largest number fall under the age group of 20 to 50 years, and the incidence of liver abscess among Hindus is about twenty times that in Muslims. Males are much more commonly affected with liver abscess than females.

In six out of 15 cases of liver abscess specially investigated at autopsy there was no evidence of recent intestinal lesions. Multiple abscesses were present in 3 of 15 cases.

Deep jaundice of an obstructive type is a very rare accompaniment of amoebic abscess of the liver and an instance of this is recorded, where an encysted liver abscess caused an obstruction of a main bile duct and eventually produced biliary cirrhosis.

Encysted liver abscess may be mistaken for a solitary gumma. Rupture into the pericardium is very rare and occurs in abscess of the left lobe where it may be mistaken for tuberculous pericarditis or other pericardial effusions. One such instance is recorded. A case is also described where the abscess contents entered the rectus sheath.

The authors discuss pulmonary amoebiasis, amoebic abscess of the brain and cutaneous amoebiasis and quote cases from the experience of other workers : none of these conditions is recorded in their own series. *P. Manson-Bahr*

SEN, N. C. **Amoebic Vaginitis.** *Brit. Med. J.* 1949, May 7, 808.

Amoebic vaginitis is rare and the author refers briefly to the available literature [see this *Bulletin*, 1944, v. 41, 44, 133 ; 1945, v. 42, 38 ; 1946, v. 43, 42]. He then reports the case of a Nepalese woman of 35 complaining of a profuse seropurulent vaginal discharge, with some soreness in the vulva and vagina and a burning sensation during micturition. The discharge was almost continuous and unrelated to menstruation.

The discharge had been present for some 4 to 5 months : about one month before it was noticed the patient had had a severe attack of dysentery (presumably amoebic), for which non-specific treatment had been given elsewhere.

Pelvic examination showed slight swelling of the right labium, the cervix and the uterus, which was soft and anteverted. There was a small ulcer in the fourchette, many linear ulcers lying mostly transversely in the mucosa of the vagina, and extensive ulceration of the cervix. The ulcers were punched-out, with overhanging edges and raw bases.

Many active forms of *Entamoeba histolytica* were found in smears of the vaginal discharge, from scrapings of the ulcers and from the discharge obtained by milking the urethra. Cysts of *E. histolytica* were found in the stools, but no ulcers were found in the lower ano-rectal canal. The liver was enlarged and tender and the descending and iliac colon was thickened.

Emetine (1 grain daily intramuscularly) was given to a total of 12 grains (in 15 days), together with local saline douches. After five days, discharge and discomfort were relieved, the ulcers were almost healed and the cervix was returning to normal. A few round and sluggish forms of *E. histolytica* were found in the aspirated cervical discharge : similar forms were found in a catheter specimen of urine. No local treatment was given for an accompanying cystitis, but emetine was continued, followed at night by stovarsol vaginal compound and an alkaline mixture.

The ulcers healed completely in two weeks, the symptoms and discharges disappeared and the patient felt quite well.

The diagnosis of amoebic vaginitis is based on the presence of the vegetative forms of *E. histolytica* in the discharges and the ulcers, the response to amoebicidal drugs and the morphological character of the ulcers.

The author suggests that infection of the vagina is by continuity with the ano-rectal canal : the method of ablution after defaecation as practised in Bengal would no doubt help mechanically. The uterus is often enlarged and it may well be infected in some cases also. It is suggested that leucorrhoea due to *E. histolytica* may be fairly common in India and should be constantly borne in mind.

H. J. O'D. Burke-Gaffney

VAN STEENIS, P. B. Enkele opmerkingen over de behandeling van amoebendysenterie en amoebiasis. [**Observations on the Treatment of Amoebic Dysentery and Amoebiasis.**] *Nederl. Tijdschr. v. Geneesk.* 1949, Jan. 8, v. 93 (i), No. 2, 105–11. English summary (3 lines).

A brief review and discussion of the drugs in use.

EL-GHAFFAR, Y. A. **The Combined Use of Sulfasuccidine and Diodoquin in the Treatment of Amoebic Infections of the Intestine.** *J. Roy. Egyptian Med. Ass.* 1949, Jan., v. 32, No. 1, 24–8.

The theme of this paper is based on the belief that bacterial infection of the intestines is an important contributory factor to the pathology of amoebiasis.

On this basis, sulphasuxidine and diodoquin were given to 36 patients with acute and 50 with chronic amoebic dysentery.

The first group manifested the usual symptoms, frequent blood and mucus stools, tenesmus and colic. The symptoms associated with the second group were varied and included a variety of obscure abdominal pains and discomforts. The faeces usually contained *E. histolytica* cysts. Sulphasuxidine was given in doses of 3–4 tablets (0·5 gm. each) three times daily for 15 days, and diodoquin, 3 tablets (0·21 gm. each) three times daily for 20 days. The anti-amoebic drug was given simultaneously with the anti-bacterial drug so as to enable it to exercise its inhibitory effect on the bacteria.

The patients with acute infections responded rapidly. No relapses have yet been reported though the first patient received treatment seven months previously. Results in chronic cases were variable. Improvement was marked in half of them. A few who relapsed quickly responded when treatment was resumed. Some in whom improvement was not very satisfactory received another course 2–3 weeks later " with better result ". Pruritus ani occurred in a few cases and Paramibe, a preparation of the same chemical constitution as diodoquin was substituted : no untoward effects were observed.

P. Manson-Bahr

Crosnier, R., Bernier, G., Molinier, A., Besseige, H. & Lefebvre, P. Prééminance thérapeutique de la conessine dans l'amibiase aiguë. [**High Therapeutic Value of Conessine in Acute Amoebiasis.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1949, Nos. 9/10, 386–92.

The authors advocate a gross dosage of 5 gm. to 6 gm. of conessine, given by mouth, according to the tolerance of the patient ; they stress the fact that under no circumstances must the daily dosage exceed 0·5 gm. ; the daily dosage is decreased as treatment progresses over a period of two weeks. Adjuvant treatment consisted of the administration of calcium gluconate in 1 gm. doses intravenously daily ; gardenal was given as necessary ; and a salt of quinine was also given " as a general tonic, to neutralize the nervous phenomena, and as an antimalarial."

Conessine can be given with impunity when there are signs of emetine poisoning ; emetine-resistant infections are susceptible to it ; there are no contra-indications to its use, as it causes no serious toxic action, but it should always be given under close medical supervision ; the recommended course of treatment must strictly be adhered to. Conessine can be given intramuscularly in doses of 0·1 gm. ; the injections are painless owing to the local anaesthetic properties of the drug, but there is local necrosis ; while intramuscular injection is not advised, it may be resorted to in cases of alimentary intolerance.

One hundred and twenty-eight cases of intestinal amoebiasis were treated with conessine ; 12 of them were cyst-passers. One hundred and fifteen (68 per cent.) of these were cured of their infections. The " cure " was consolidated in most cases by a repetition of the course, but of the 44 patients re-treated 9 were found still to be infected and another 3 subsequently suffered attacks of acute amoebic dysentery. It is concluded that the treatment gave a cure rate of 89 per cent. Nineteen cases of amoebic hepatitis were treated, apparently with satisfactory results, with conessine.

Various suggestions are made on further lines of investigation of the action of conessine in amoebiasis, which the authors state to be equal, or superior, to emetine.

A. R. D. Adams

Siguier, F., Crosnier, J. & Sapin-Jaloustre, H. Amibiase hépatique surinfectée probable. Echec du traitement mixte émétine-conessine-pénicilline. Guérison par l'association émétine-streptomycine. [**Probable Secondary Infection in a Case of Hepatic Amoebiasis. Failure to respond with Combined Emetine-Conessine-Penicillin Treatment and Cure with Emetine combined with Streptomycin.**] *Bull. ét Mém. Soc. Méd. Hôpit. de Paris.* 1949, Nos. 13/14, 620–24, 3 figs.

Manson-Bahr, P. **The Treatment of Amoebic Liver Abscess with Chloroquine.** *J. Trop. Med. & Hyg.* 1949, May, v. 52, No. 5, 91–3, 1 chart. [10 refs.]

While emetine combined with emetine bismuth iodide is usually effective in the treatment of hepatic amoebiasis, there is a residue of cases of liver abscess in which these drugs fail to act.

The author refers to the use of chloroquine in hepatic amoebiasis and suggests that it probably acts by concentration in the liver parenchyma [for experimental observations on animals regarding relative concentrations of emetine in the liver and intestine, see this *Bulletin*, 1948, v. 45, 1004].

The history and pharmacology of chloroquine and related substances are discussed and reference is made to two published accounts of its use in hepatic amoebiasis. Conan [this *Bulletin*, 1948, v. 45, 430] reported rapid disappearance of clinical manifestations in six cases of hepatic amoebiasis, but a persistence of *E. histolytica* in the stools of 13 out of 28 patients having intestinal amoebiasis after treatment with chloroquine: as the drug is almost entirely absorbed from the gastro-intestinal tract, its effect on intestinal amoeba is attributed to plasma or tissue concentration.

Murgatroyd and Kent demonstrated a case at a Laboratory Meeting of the Royal Society of Tropical Medicine and Hygiene (*Trans. Roy. Soc. Trop. Med. & Hyg.*, 1948, v. 42, 15) in which trophozoites of *E. histolytica* were present in the liver pus, but were resistant to emetine. On the fifth day of treatment with chloroquine (0·25 gm. thrice daily by mouth for 18 days) the amoebae disappeared and by the twelfth day, the abscess cavity had healed. The patient was well enough to be discharged from hospital two weeks after completion of the course and was prescribed a maintenance dose of 0·25 gm. chloroquine twice a week for 3 months (in this case the discharging liver abscess had been opened 4 months before and had also resisted treatment with penicillin and streptomycin given to deal with secondary infections present).

In the case under review, the present author treated a European patient suffering from an advanced amoebic abscess of the liver, who had been interned in Siam for 3½ years. He had no history of amoebiasis but in 1948, two years after he returned to Calcutta, symptoms of this condition began. Clinical and radiological evidence suggested that he had subacute hepatitis complicated with early pulmonary tuberculosis. He was given a course of streptomycin, with no apparent effect on his pyrexia. Later, he became worse and the manifestations of amoebic abscess of the liver became evident. In October, 1948, in Madras, he was given emetine and penicillin, and 1½ pints of amoebic pus were removed from his liver. On arrival in Britain he was extremely ill and the evidence of liver abscess was still marked. No amoebic cysts were found in the stools.

There was no adequate response to emetine, followed by emetine bismuth iodide. Chloroquine was then given and the temperature chart (reproduced in the paper) showed an almost immediate response. The temperature became normal and the signs less apparent: however, pyrexia began again some 10 days later, but yielded to renewed chloroquine therapy. Progress was then uninterrupted and the patient is now in good health.

The first course of chloroquine diphosphate consisted of 4 gm. over eight days and the second of 4·75 gm. over 16 days. The priming dose was 0·75 gm. (0·45 gm. base) followed by a sustained dose of 0·3 gm. daily and later 0·5 gm. (0·3 gm. base) daily. No toxic effects were observed. Half the amount of chloroquine appeared to be equally effective in controlling the fever during the second course. *H. J. O'D. Burke-Gaffney*

LEPROSY.

Sen, P. **Leprosy in Calcutta.** *Internat. Med. Abstracts & Reviews.* Calcutta. 1949, Jan., v. 5, No. 1, 20–23.

This note gives data regarding the incidence of leprosy in Calcutta as compared with adjacent districts, and discusses the suitability of the city for the proposed all-India Leprosy Institute. Surveys of the disease in cross sections of the Calcutta population showed that the incidence varied between 0·3 and 1·65 per cent. with an estimated rate of 0·5 per cent. ; or 20,000 in a population of 40 lakhs (4 millions) including the suburbs. Work in the four Calcutta clinics showed over 10,000 leprosy patients as permanent residents ; some Calcutta dermatologists consider this to be an underestimate. A table shows the estimated number of leprosy cases and the rate per thousand population in the districts of Western Bengal, which are all higher than in Calcutta, but the author thinks that the greater density of cases makes them more dangerous in Calcutta. In the latter part of the paper he advocates Calcutta as the best site for the all-India Leprosy Institute on account of the laboratory and other medical facilities and a leprosy hospital with nearly 200 beds for permanent patients. [This opinion ignores the great advantages of an agricultural colony with ample land for cultivation and for housing far larger numbers of cases than Calcutta can provide for, with greater facilities for testing new drugs on in-patients under close observation.] *L. Rogers*

Tisseuil, J. Sur 3 inoculations positives de la lèpre humaine au rat d'élevage. [**Successful Inoculation of Human Leprosy into Rats.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 11/12, 649–52.

The author has in three instances, out of a number, succeeded in inoculating human leprosy into rats. In the first positive experiment, an emulsion of leproma from an Argentine patient was injected into the testis of 20 rats. A small yellow lump in the testis of one of them was grafted under the skin of another rat and produced a nodule, sections of which showed very numerous bacilli. Passages into the testicles of three other rats were negative. In the second experiment, ten rats were injected with suspensions of lepromata and the surviving rats were re-inoculated from a leproma five months later and after six more weeks a nodule with a caseous centre was inoculated into each flank of another rat, which resulted in a nodule very rich in bacilli, and further passages of the bacilli were obtained. In the third positive experiment, 10 rats were placed in an hermetically sealed chamber contaminated by pulverized lepromata and one of the rats killed 15 months later showed miliary nodules and a little caseous material in the lungs rich in bacilli, which could not be cultivated on Löwensteins's medium. Inoculation into a guineapig caused a general infection free from evidence of tuberculosis. Five rats inoculated at the same time were killed eight months later and all of them showed gross lepromata at the site of inoculation.

The author then discusses criticisms of his work, especially the occurrence of spontaneous rat leprosy, and without under-estimating them he considers it was useful to record his experiments to help others with regard to such inoculations. *L. Rogers*

KIANG, Sadie & CHOA, G. H. **The Blood Picture in Leprosy.** *Amer. J. Med. Sci.* 1949, Mar., v. 217, No. 3, 269–76. [13 refs.]

Previous literature shows differences of opinion regarding the blood changes in leprosy, so the authors, in China, have carried out estimations in 36 cases which had not recently been under treatment. Those showing helminthic infections were treated before the blood was examined. The authors did not find that promin treatment had much effect on the blood except in causing some reduction in the haemoglobin, but the red and white corpuscle counts were little affected by the drugs used. Both lepromatous and neural cases were included, but patients with intercurrent diseases were excluded. The results are shown in tables and include the following data: Wright's stain and the Wintrobe haemocrit were used, and the results are compared with the standard figures of Wintrobe and with those of Chinese workers, which do not deviate much from the general average. Anaemia was rather constant but in no case severe. Macrocytic and normocytic anaemias were met. Reticulocyte counts were distinctly low and they varied between 0·2 and 0·9 per cent.; this the authors are unable to account for. The sedimentation rate was raised in all but four and averaged 19 mm. Leucocytosis of a moderate degree was present in 10, or 27·7 per cent., chiefly in advanced lepromatous cases. Only two showed moderate leucopenia. The neutrophile count was definitely deviated to the left, but this is usual in the Chinese so it is not significant. High eosinophile counts were a notable feature, even when the stools had become negative as regards helminths, so they consider this related to the disease especially in its lepromatous form, in which type it chiefly occurred. Monocytosis and lymphocytosis showed a high incidence with 19 cases, or 52·2 per cent. of each, which is not surprising in such a chronic disease as leprosy. During their two years' work there was no clinically marked flare-up or deterioration resulting from treatment among the severe cases. Neither lymphocytosis nor monocytosis appeared to have any prognostic value, but the authors agree with other workers that they may be useful indicators of the presence of leprosy. *L. Rogers*

DHARMENDRA. **A Note on the Histopathology of Leprosy.** *Internat. Med. Abstracts & Reviews.* Calcutta. 1949, Jan., v. 5, No. 1, 5–8.

FLOCH, H. & CAMAIN, R. Aspects histopathologiques de la lèpre en Guyane française. [**Histopathological Aspects of Leprosy in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 176.* 1948, July, 7 pp.

The authors in French Guiana record work during one and a half years on the histology of leprosy, including the effects of sulphone treatment. In the first place they agree that the histological changes in "indifferent" [or "intermediate uncharacteristic", see this *Bulletin*, 1947, v. 44, 1073], tuberculoid and lepromatous cases are of diagnostic importance. They also agree with the observations of FITE and GEMAR concerning the histological changes in cases improving under sulphone treatment and bring out the following points. In lepromatous cases under sulphones, interesting regressive changes occur in the epithelium and other tissues. The vacuolated cells become less numerous, infiltration with lymphocytes is seen and the spongiocytes

diminish in numbers. With the atrophy of the nodules, connective tissue cells predominate. On the contrary, in " indifferent " and tuberculoid forms the histological appearances are not affected by sulphones.

Sections are better for determining the changes in the number and appearances of the lepra bacilli than are teased specimens. The examination of at least four sections is recommended. By this method the percentage of bacteriologically positive cases is raised to 31 of " indifferent " and to 29 in tuberculoid minor and to 88 in reacting tuberculoids, so that in tuberculoid cases when examined in stained sections the organisms are more frequently found than by former methods. Under sulphone treatment the lepra bacilli become much decreased in numbers, show morphological changes and do not stain as well, especially those in the neighbourhood of blood vessels. This, the authors think, explains the resistance of " indifferent " and tuberculoid cases to sulphones, because in these forms there is less vascularity and many of the organisms are protected from the action of the drugs by being situated in nerve trunks, which the sulphones reach with difficulty. *L. Rogers*

Cochrane, R. G. **Some Brief Comments on the Classification of Leprosy.** *Internat. Med. Abstracts & Reviews.* Calcutta. 1949, Jan., v. 5, No. 1, 2–5.

Cochrane, R. G., Ramanujam, K., Paul, H. & Russell, D. **Two-and-a-Half Years' Experimental Work on the Sulphone Group of Drugs.** *Leprosy Review.* 1949, Jan.–Apr., v. 20, Nos. 1/2, 4–64, 15 figs. & 1 chart. [14 refs.]

This long paper records brief notes on 54 cases of leprosy treated by sulphones in South India in the course of two and a half years. Most of them were given diasone or sulphetrone orally with very similar results to those recorded previously by a number of leprologists. Of greater interest are six cases given injections of sulphetrone with very similar results to those obtained after its oral administration, but obtained with a total average dosage of 81 grammes in place of an average of over 3,000 grammes by oral use ; a very material saving in cost per case. A discussion of the whole series with a comparison with hydnocarpus oil treatment brings out the following points, including the effects of injections of the much less expensive sulphone, diamino-diphenyl-sulphone, in eleven cases. Good photographs of six cases before and after treatment are given, but unfortunately the table relating to them does not give the number of pages referred in the text in the case of two, and in two others such data do not appear to correspond with those in the text. The first part of the paper concludes that for oral use sulphetrone is superior to diasone ; a conclusion others had previously reached. About 30 per cent. of those treated with diasone showed reactions, but they later subsided in spite of the drug being continued without rest and they did not recur in any cases after 1000 tablets had been given. Furthermore, under this drug the only cases that became negative were in boys who received relatively large doses, so maximum dosage is indicated, but the high cost rarely allowed more than 4 tablets a day to be given. With oral sulphetrone only one patient had a very severe reaction and foot drop followed. Four of the nine became negative within two years.

Owing to the high cost of diasone and sulphetrone given orally, which prohibits its use on a large scale, and the necessity of giving daily intravenous doses of promin, the author has tried injection of sulphetrone with interesting results. The active principle of all three, namely, sulphone or diamino-diphenyl-sulphone has also been tested by injection, but the case notes and comments show that the latter gave rise to more severe reactions. Treatment by sulphones in general is also compared with that by the injection of hydnocarpus oil. The best results were obtained by subcutaneous injections of 7 cc.

of 50 per cent. sulphetrone in water twice a week. On the other hand sulphone in doses of 1 to 1·5 gramme a week in a strength of 25 per cent. suspension in groundnut oil is probably the most potent remedy, but one which produces severe reactions in the form of anaemia, giddiness and sickness, and peripheral neuritis, sometimes of an alarming degree ; this prohibits its use on a large scale until a safe dosage is found. In early lepromatous cases, hydnocarpus treatment is the best. This paper should be studied by all interested in leprosy treatment. *L. Rogers*

Floch, H. & Camain, R. Sur le traitement de la lèpre par les sulfones en Guyane française. [**Treatment of Leprosy by Sulphones in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 179.* 1948, Sept., 11 pp. [14 refs.]

As in French Guiana lepromatous cases constitute only one-third of the total cases, the sulphone treatment had been used in all three types with interesting results. Both promin and diasone have been used in doses advised by early American workers in patients under the age of 20 years as a rule. Details are given of some of the cases and the following are the main conclusions arrived at after treatment for eight to eighteen months. In lepromatous cases retrogression was noted as described by earlier workers. In nine " indifferent " forms improvement was noted in six, aggravation in two and no change in one, so the results were less clear than in the lepromatous type. Some degree of improvement in nerve symptoms was also noted. In three tuberculoid cases after 20 months two were stationary and one was aggravated. The histological and bacteriological changes were as described in the above paper by the same authors. Any signs of anaemia were easily controlled by iron. In only three lepromatous cases were reactions seen. The authors consider that the action of sulphones is to destroy the lepra bacilli in the more vascular lesions as well as those which enter the blood stream. *L. Rogers*

Floch, H. & Camain, R. Sur le traitement de la lèpre en Guyane française par les dérivés sulfonés. [**Sulphone Treatment of Leprosy in French Guiana.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 11/12, 646–9.

The authors report on trials of promin and diasone during sixteen months. They were used in doses and with intervals similar to those in the case of the original trials at Carville and moderate degrees of anaemia met with were readily controlled by iron. Only a few slight reactions were met and they subsided readily. Diasone was not well borne by some patients. Promin was used in three tuberculoid and thirteen indifferent [undifferentiated] cases in children, with no clinical improvement except in two pre-lepromatous indifferent cases, in which histological examinations showed some atrophy of active areas with round cell infiltration and return to the indifferent type, but little change was found in frankly indifferent cases. In the case of nine lepromatous cases there was a definite slow retrogression of the clinical symptoms in the following order. First nasal and conjunctival signs disappeared, next atrophic ulcers healed, followed by decrease of lepromata and dermal infiltration, which was slowest in the case of the ears, and lastly improvement in sensation occurred. Further the mental outlook of the patients and their general condition much improved. Microscopically the lepromatous structure was gradually replaced by connective tissues and in one case there was a return to the indifferent type. The lepra bacilli became much reduced, granular forms became dominant

and in one case the granules were no longer alcohol-acid resistant. In three cases treatment had to be given up on account of gastric troubles and headache. Thus the results were favourable in lepromatous cases. *L. Rogers*

GRILLO, J. Ueber die Wirkung des Streptomycins auf Lepra. [**The Action of Streptomycin in Leprosy.**] *Ztschr. f. Hyg. u. Infektionskr.* 1948, Apr. 1, v. 127, Nos. 6/8, 588–91, 2 figs.

This is a report on the successful treatment of an advanced case of leprosy by streptomycin : the case was classified as L2N2 with numerous lepromata of different sizes on the face and arms and elsewhere, together with hyperpigmented patches and anaesthetic zones and ulcers on the extremities. Streptomycin was first given in doses of two to three grammes and produced a strong febrile reaction with deterioration in all the skin lesions. All the lepromata increased in size and became softened. Lepra bacilli in the nasal mucus and the lymphatics appeared to be increased in numbers ; the reaction lasted ten days and was followed by definite and progressive improvement with steady retrogression in all the lepromata. Suppurating ulcers gradually cleared and healed in a normal manner without the production of pigmentation and the action of the streptomycin was favourable regarding all the other symptoms of the disease. The treatment was continued until a total of 300 grammes of streptomycin had been given. Later the daily dose was 4 grammes, and then it was reduced to 3 and 2 grammes and the intervals between the injections from four to six hours ; the total amount of the preparation given was 360 grammes. The toxic symptoms noticed included slight febrile reactions, skin eruptions, nausea, giddiness, and albumin and casts in the urine, but they were not sufficiently severe to necessitate interruption of treatment or decrease in the dosage.

The results of the treatment are illustrated by photographs before and after, which show disappearance of numerous nodules from the face and ears, and the author records that almost all the lepromata were reabsorbed, so that after three months the majority had completely disappeared. Thus the deterioration in the lesions during the early strong reaction was succeeded by steady fading of the reactionary symptoms and subsidence of the lesions. The ulcers of the nasal mucous membrane also healed in a surprisingly short time and suppurating skin ulcers lost their pyogenic flora and healed in normal manner without showing any tendency to relapse. Hyperaemic patches on the body diminished and faded. During the treatment bacteriological examinations were repeatedly made and showed changes in the morphology and staining properties of the lepra bacilli. Granules first appeared in them and later numerous coccal forms appeared and short rods, which gradually lost their acid-fastness, so that at the end of the treatment only exceptional, weakly-staining involution forms were evident and they were very difficult to stain, which is regarded as due to protoplasmic changes. [These changes resemble those described by the reviewer and illustrated by a coloured plate, in 1917 (this *Bulletin*, 1918, v. 11, 407), following reactions in nodules resulting from the injection of sodium hydnocarpate.] *L. Rogers*

MARIANO, J. A leprolina " Souza-Araujo " no tratamento da lepra. [**De Souza-Araujo's Leprolines in the Treatment of Leprosy.**] *Mem. Inst. Oswaldo Cruz.* 1948, Mar., v. 46, No. 1, 285–93, 2 figs. English summary.

The author starts his account by recording comparative tests of the reactions to lepromin and leproline. (1) In 16 nerve leprosy patients lepromin elicited a positive in 13, negative in 3 ; leproline 12 and 4 respectively. (2) In 75

lepromatous cases lepromin was negative in 72, positive in 3; leproline negative in 59, positive in 16. (3) Among 20 "healthy" persons lepromin gave a positive in 13, negative in 7; leproline 12 and 8 respectively.

Leprolines, he states, are of value prognostically as offering a method of gauging the tissue reactions, if the dosage be standardized and regulated. Finally, details of four lepromatous patients treated with leproline preparations partly intravenously every 6 days, partly intramuscularly and partly intradermally, are given. At first, fever up to 40°C. might follow injection, lasting for 4–6 hours, and in all four the Mitsuda reaction was changed from negative to positive.

H. Harold Scott

DE SOUZA-ARAUJO, H. C. Novo agente terapêutico da lepra: as leprolinas "Souza-Araujo". Os resultados de cinco anos de experiências: 1943 a 1948. [**De Souza-Araujo's Leprolines in the Treatment of Leprosy. The Results of their Use in the Five Years 1943–48.**] *Mem. Inst. Oswaldo Cruz*. 1948, Mar., v. 46, No. 1, 233–54. [14 refs.]

Compared with chaulmoogra it is perhaps correct to regard leprolines as a "new therapeutic agent" for leprosy though they have been in use for 5–6 years. Leprolines are "antigens" prepared by Professor de Souza-Araujo from acid-alcohol-resistant organisms grown from human leprosy lesions or from insects which have been allowed to feed on such patients. For treatment, the material is administered intravenously and intracutaneously. The results reported are said to be: improvement in the general condition, in appetite and in sleep; reactivation of lepromata, some suppurating, others being absorbed in "a fairly short time"; making the Mitsuda response strongly positive; improvement of the ocular and laryngeal lesions. In the present paper details are given of 16 patients so treated. [See also this *Bulletin*, 1945, v. 42, 132, 133, 1010, 1011.]

H. Harold Scott

DE SOUZA-ARAUJO, H. C. As leprolinas "Souza-Araujo" e a sua rápida acção terapêutica nos males perfurantes plantares lepróticos. [**The Results of Leproline Treatment in Perforating Ulcer of the Foot in Leprosy.**] *Mem. Inst. Oswaldo Cruz*. 1948, Mar., v. 46, No. 1, 255–67, 5 figs. English summary.

Illustrations of the growth of cultures of acid-alcohol-fast organisms from guineapigs and white rats are reproduced, from which leprolines are prepared. Brief notes of 21 patients are given who had perforating ulcers of the foot and were treated by Cassiano in the Baurú Leper Colony of São Paulo and of 5 under the author's own observation. In Dr. Cassiano's patients the average total amount of leprolines injected was 7·7 cc. and the duration of treatment 23 days. Eighteen of the patients remained cured 18 months later, 3 had relapsed after cicatrization; a man of 28 years relapsed 3 months after treatment ceased, a woman of 54 after 3½ months and another woman of 29 years after 10 months. Reference is made, but without details, to 50 such patients treated by Dr. Caldeira in a colony in Minas Gerais; 46 were recorded as cured.

H. Harold Scott

JAGADISAN, T. N. **If To-Morrow we were sure of a Specific for Leprosy?** *Internat. Med. Abstracts & Reviews*. Calcutta. 1949, Jan., v. 5, No. 1, 28–30.

RAMAKRISHNAN, N. **Welfare Work for Leprosy Patients.** *Internat. Med. Abstracts & Reviews* Calcutta. 1949, Jan., v. 5, No. 1, 25–8.

Yčas, J. Die Lepra in Estland, Livland und Kurland bis 1914. **[Leprosy in Esthonia, Livonia and Courland up to 1914.]** *Ztschr. f. Hyg. u. Infektionskr.* 1948, Apr. 1, v. 127, Nos. 6/8, 825–58, 2 figs. [50 refs.]

HELMINTHIASIS

Brackett, S. & Bliznick, A. **Screening Large Numbers of New Chemical Compounds for Anthelmintic Activity using Infections with *Nippostrongylus muris* in Mice.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 8–18. [22 refs.]

For screening drugs of the trichloroacetamide group and compounds related to it, young mice of about 4 weeks old were infected with *Nippostrongylus muris* by intraperitoneal injections with infective larvae. About 500 larvae were used for each mouse, of which more than 20 per cent. usually developed to maturity.

Test compounds were mixed with the diet in a strength of 0·5 per cent. by weight and given to infected mice in groups of three during a period of 8 days, *i.e.*, from the time of inoculation with larvae to the date of autopsy. Evidence of the activity of the drug was estimated by the presence or absence of worms in the intestine on the 8th day of infection.

Standard anthelmintics when administered under this régime did not exhibit much effect on *N. muris*, but trichloroacetamide and related compounds were most effective against developing worms but almost or completely ineffective against mature worms. Tested against other helminth infections, *e.g.*, those due to *Strongyloides ratti*, *L. carinii*, oxyurids, *S. mansoni*. *H. nana* and *T. spiralis*, trichloroacetamide was without effect. *J. J. C. Buckley*

Gitlin, G., Schaffer, S. & Gunn, C. S. **Intestinal Helminth Infection : Incidence in Patients attending the Springfield Health Centre, Durban.** *South African Med. J.* 1948, Dec. 25, v. 22, No. 24, 788–93. [20 refs.]

Routine stool examinations were carried out at a health centre in Durban. The data over a period of about one year have been analysed. Only the findings in the first stool examined are recorded ; saline and iodine preparations were examined ; and no concentration methods were used.

The subjects were divided into three racial groups, Indians (399), Africans (613) and " coloured " (415) ; the helminthic infection percentages were 68, 57 and 65, respectively. The only frequent findings were *Ascaris* (48 per cent.) and *Trichuris* (36 per cent.). Hookworm ova were found in 1·1 per cent., *Taenia* ova in 1·3 per cent., and *Strongyloides* larvae in 0·4 per cent. Other findings were *Schistosoma mansoni* (2 cases), and *Enterobius vermicularis*, *Hymenolepis diminuta* and *H. nana* (1 each). *Taenia* ova were not found in Indians. Of the 62 per cent. of persons with helminthic infections nearly half (38 per cent.) had multiple infections, usually *Ascaris* and *Trichuris* ; the highest percentage of multiple infection occurred in the " coloured " group. Detailed tables are given and their significance discussed.

A comprehensive table of the percentage findings of other helminthological surveys in South Africa is given. The authors' figures are not materially different from those of others where comparable methods were used.

L. E. Napier

JAFFÉ, R. Parasitosis intestinal como causa de muerte en Venezuela. [**Intestinal Parasites as a Cause of Death in Venezuela.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Apr., v. 10, No. 2, 283–92. [17 refs.]

The author has conscientiously tried to separate patients dying *with* and those dying *from* helminthic infestation. Many persons harbour *Ascaris*, for example, in large numbers without serious harm, whereas others with fewer may, owing to migration of the worms, or to their position, die from, say, liver abscess or suppurative cholecystitis. Again, *Necator* is common, but among 3,700 autopsies the author found 14 in which he is convinced death was due to this infestation, the worms were present in " enormous numbers " and there was fatty degeneration of the heart and intense anaemia. He does not exclude those who died as a result of taking carbon tetrachloride, regarding such a fatality as due, though indirectly, to the infestation. The cause and effect sequence is less clear in some of the cases recorded ; for example, a child of 7 years with innumerable *Trichuris* in the large intestine and a fatty liver, for the child had also tuberculosis of the hilar glands and of the spleen and schistosomes in the portal vein. Another had *Ascaris* and schistosomes also. *Enterobius vermicularis*, if in large numbers may cause death, says the author, but only indirectly through cachexia and secondary infection.

H. Harold Scott

BARLOW, C. H. Une théorie sur la ponte de Bilharzia haematobia. [**A Theory concerning Egg Deposition by** *Schistosoma haematobium.*] *Ann. Parasit. Humaine et Comparée.* 1948, v. 23, Nos. 5/6, 301–4.

This theory is concerned with the method of egg deposition in the bladder wall by *Schistosoma haematobium* and the escape of the eggs to the lumen of the bladder. It is suggested that the female worm penetrates the capillary in which she is lying and lays her eggs in a small pocket or cyst in the bladder wall close to its inner surface. Having filled the cyst with eggs she retires to the capillary, leaving a canal between capillary and cyst through which she returns again to refill the cyst with eggs when it has emptied itself. The eggs escape during micturition which causes the rupture of a weak point in the bladder wall near the cyst.

The theory is supported on various grounds. It is argued that if the eggs make their way slowly and fortuitously through the tissues from various levels, according to the procedure generally accepted at present, they would be at different stages of development on arrival in the bladder lumen, but this is not the case. The constant numbers of eggs which daily appear in the urine is also held to conform more with the new theory than with the old.

Clinical data in support of the theory are adduced from the results of examining urine collected during a single micturition in a series of centrifuge tubes of 50 ccm. capacity. It was noted that (1) the first part of the urine was clear, with only a little fresh blood ; (2) the next portion contained blood and a number of conical plugs of clotted blood which enclosed a few eggs, mostly with inactive miracidia. Their appearance corresponded with the rupture of the cysts before the eggs are discharged ; (3) the next portion contained much blood and some eggs. Evidently after the blood clots are expelled profuse bleeding occurs ; (4) the last portion was inundated with eggs, forced out of the cysts by muscular contraction of the bladder wall. The same sequence of events was observed with several repetitions of this procedure and also with the author's own bilharzial infection.

Evidence that the adult worms are situated very close to the spot where the eggs are evacuated from the tissues, was to hand from the author's own infection, in which a number of papules on the anal skin were found to be full

of eggs. Biopsy disclosed a pair of worms just under the skin close to the papules. It is held that in experimentally infected animals it is impossible to demonstrate the true position of the adult worms, as the worms have time to retire inwards during the process of killing the experimental animal and fixing the tissues.

The theory thus has much to recommend it but is unsupported by histopathological evidence. The extra-capillary mode of egg deposition especially requires corroboration in view of the known facts regarding intra-capillary deposition. *J. J. C. Buckley*

HALAWANI, A., HAFEZ, A., NEWSOME, J. & COWPER, S. G. **Miracil D: Effect on *B. mansoni in Vitro* and in the Treatment of Urinary Bilharziasis.** *J. Roy. Egyptian Med. Ass.* 1949, Jan., v. 32, No. 1, 29–51, 1 fig.

Adults of *Schistosoma japonicum* have already been shown to survive *in vitro* for considerable periods [this *Bulletin*, 1939, v. 36, 35 and 41]. Egyptian gerbils are readily infected with *S. mansoni*; worms of this species were removed aseptically from the liver, gut and mesentery of infected gerbils and transferred to Carrel flasks containing 1·5 to 3 ml. of sterile medium and incubated at 37°C. The media were (1) human serum and Tyrode solution containing a drop of laked blood and 10 units of penicillin per ml.; the *p*H was adjusted to 7·2; (2) normal serum and penicillin; and (3) serum from patients receiving Miracil D. In Miracil-free media, worms survived 14 to 20 days; the haemoglobin vanished in 4 or 5 days; bacterial contamination curtailed the survival of the worms. In Tyrode solution containing 0·5 mgm. of Miracil D per ml. the worms survived from 2 to 3 hours; in a concentration of 4 mgm. of the drug per ml. they died rapidly. In normal serum containing 3 mgm. of Miracil per ml. the worms were apparently unaffected by the drug during an observation period of 4 days; bacterial contamination then ended the experiment. In serum, changed daily, from a patient receiving Miracil, which contained up to 5 mgm. of the drug per ml. the worms survived for 4 days.

Twenty prison guards, suffering from *S. haematobium* infections and having haematuria, who had not been re-infected for 6 months before treatment, were treated with Miracil D. Fifteen of them received between 8·3 and 9·8 gm. of the drug by the mouth over a period of 8 days; five had between 5·6 and 6·6 gm. over 5 days. The total dosages in the first group ranged from 111 to 136 mgm. per kgm. of body weight, and those in the second group from 85 to 95 mgm./kgm. Estimations showed that the drug blood-level in 10 of the patients rose to a peak, usually by the 4th or 5th day; thereafter there was a slight decline, and a plateau of between 4 mgm. and 6 mgm. per ml. was maintained until the 9th day; in some cases a level of 4 mgm. was still evident on the 14th day in cases treated for 8 days.

Side effects of the treatment were a burning sensation in the mouth, oesophagus and stomach, with nausea and, occasionally, vomiting; giddiness; and yellow staining of the skin; in some cases there was pain in the chest. By the 4th or 5th day of treatment these diminished. The eosinophil count rose sharply during treatment in some cases, but there was no other change of significance in the blood picture. There was no real indication of changes due to impairment of the heart, liver or kidney functions. Gross haematuria stopped in all cases within 5 days of beginning treatment. Six of the 15 patients receiving the 8-day dosage, and three of the five on the 5-day dosage, were still passing living ova in the urine, albeit reduced in number, 3 weeks after treatment. Re-examination at the end of a period of 2 months after treatment

showed that all patients but one in each scale of dosage were passing viable ova, though there is an " impression " that the number was less than initially.
A. R. D. Adams

JANSSEN, P. La bilharziose intestinale dans la région de Toro (province orientale du Congo belge). [**Intestinal Schistosomiasis in Tora, Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1948, Dec. 31, v. 28, No. 4, 395–410, 1 pl.

During a stay of two-and-a-half years in Tora, which is situated on the border of Haut-Ituri in the Eastern province of the Belgian Congo, studies were undertaken of the schistosomiasis prevalent in the region. The area is a gold-mining one, with over two thousand Africans employed in the industry. Much water is needed, and this is stored in large shallow barrages, rich in vegetation, interconnected by canals. The conditions are therefore peculiarly suitable for snail propagation, and *Planorbis* is very plentiful. Microscopical examination, usually of single specimens of stool, showed 287 of 411 otherwise apparently healthy Africans to be passing *Schistosoma mansoni* eggs ; 358 of these were adults, of whom 86 per cent. were found infected, and 53 were children, 75 per cent. of these being found to be infected. None of these Africans suffered from alimentary disorders ; on sigmoidoscopy of 50 persons, 25 of them known to harbour parasites, no abnormality was observed.

On physical examination, two-thirds of those known to harbour the parasite had enlargement of the liver. Tests of liver function did not prove helpful in diagnosis, and estimations of blood protein yielded inconclusive information. Biopsy showed schistosome ova in the liver to be surrounded by mononuclear cells and fibroblastic inflammatory reaction. The lesions appeared largely to be limited to a granulo-fatty degeneration immediately around the ova, and well-defined liver cirrhosis was but rarely seen. *A. R. D. Adams*

VAN DER KUYP, E. **Planorbidae Records of the Netherlands Antilles.** *Amer. J. Trop. Med.* 1949, Mar., v. 29, No. 2, 259–61. [18 refs.]

" *Tropicorbis isthmicus* Pilsbry is found on the islands of Curaçao and Bonaire. Other *Tropicorbis* species may also be present. *Australorbis glabratus lugubris* Wagner, and *Helisoma duryi intercalare* Pilsbry were imported into Curaçao from Venezuela. The *Australorbis* species was found only once in Aruba in an aquarium. Autochthonous cases of schistosomiasis have never been reported from the Netherlands Antilles."

SCHREIBER, Freda G. & SCHUBERT, M. **Experimental Infection of the Snail** *Australorbis glabratus* **with the Trematode** *Schistosoma mansoni* **and the Production of Cercariae.** *J. Parasitology.* 1949, Feb., v. 35, No. 1, 91–100, 1 fig. [10 refs.]

The work described here was undertaken to obtain data of value to laboratory workers concerned with the chemotherapy of schistosomiasis in experimental animals and was designed to find out (1) the percentage of snails that becomes infected on exposure to miracidia under a uniform set of conditions ; (2) the time at which half the miracidia die under these conditions ; (3) the production of cercariae by infected snails under specific controlled conditions ; (4) the time at which half the infected snails die ; (5) the time at which half the cercariae die under a few specific conditions.

(1) Eggs of *S. mansoni* were obtained from faecal pellets passed by experimentally infected mice or hamsters and hatched after standing 1 to 2 hours in

water at 28°–30°C. Snails were exposed individually to one or to 5–7 miracidia and examined for emission of cercariae 4 to 10 weeks after exposure. Of 127 snails exposed to one miracidium each, 8 per cent. became infected. Of 1,698 snails exposed to 5–7 miracidia each, 50 to 60 per cent. became infected.

(2) Miracidia were placed in a number of beakers at 24° to 26°C. and counted at intervals of 2 hours. After about 8 hours half the original number were dead.

(3) Counts of emerging cercariae were carried out for periods of 2 months on batches of infected snails, generally about 4 or 5 times each week. The weighted average number of cercariae liberated per snail per day was 698, the range being 14 to 4,158. The liberation on Mondays (*i.e.*, after 2 days' rest from stimulation) was usually higher than on other days. Stimulation was by warming at 30°C. or by warming plus illumination. The combined stimulant increased the average emergence by 30 to 90 per cent. of the emergence produced by warming alone.

(4) The time after the first liberation of cercariae at which half the snails died was 4 weeks.

(5) All cercariae incubated at 30°C. were dead 20 hours after emergence and half were dead between 8 and 16 hours. *J. J. C. Buckley*

LUTTERMOSER, G. W. & CASTELLANOS, J. V. Observaciones sobre la propagación y la destrucción del caracol, *Australorbis glabratus* Say, 1818, vector de *Schistosoma mansoni* (bilharzia) en el Valle, D. F. [**On the Multiplication and Destruction of** *Australorbis glabratus*, **the Vector of** *Schistosoma mansoni* **along the El Valle River, Federal District, Venezuela.**] *Rev. Sanidad y Asistencia Social.* Caracas, 1945, Feb., v. 10, No. 1, 109–48, 4 maps & 6 figs. (5 on 1 pl.). [25 refs.] English summary.

This question is of much local importance because the rate of infestation among the people is high, the vector abounds and there is a heavy contamination of the water-courses and their banks with excreta and many persons use this water. A careful study extending over 3 years was undertaken to determine the prevalence of *Australorbis glabratus* in the Federal District of the State of Miranda in Venezuela. Line maps show very clearly that for long distances of the main rivers this snail is not found, but in the lower reaches of the Valle River from Turmerito to its junction with the Rio Guaire they abound, *i.e.*, in the northern hilly districts of Venezuela, and here *Schistosoma mansoni* is endemic. The river bed here is less steep and the flow is less rapid ; there is abundant algal and other vegetal growth, the sewage of the population drains into it and the water contains much bicarbonate of calcium, all conditions favourable to the propagation of the snail. In the dry season they breed copiously and in the wet season they are washed downstream to other parts.

In dealing with this problem it was found that attempts to eliminate the vector from certain areas were, however successful temporarily, ineffectual in the long run because water coming down from the upper reaches resulted in re-infestation. Two things were necessary : to prevent the passage of infected sewage into the river and to start dealing with scourge at the head-waters first and then progress gradually downstream. The intake site for irrigation must be carefully selected to prevent passage of the snails into the irrigation canals, and these canals should be lined and kept clean. Sand-filtration is not enough to remove infection from highly infested water, for guineapigs were infested by water filtered through a depth of 100 cm. of sand. Photographs are

reproduced showing the state of the terrain which allows and fosters the propagation of *Australorbis glabratus*. *H. Harold Scott*

LUTTERMOSER, G. W. Estudios sobre el caracol vector del *Schistosoma mansoni* en la ciudad de Maracay y Alrededores (Estado Aragua), con recomendaciones para luchar contra el. [**The Vector of** *Schistosoma mansoni* **in Maracay and its Environs and Recommendations for dealing with it.**] *Rev. Sanidad y Asistencia Social.* Caracas, 1945, Feb., v. 10, No. 1, 149–63, 17 figs. on 3 pls. & 1 map. English summary.

Maracay is the capital of the State of Aragua and lies north-east of the Valencia Lake. Nearly 100 places were selected for examination for *Australorbis glabratus*, the intermediate host of *S. mansoni*—rivers, drains, irrigation canals, reservoirs, etc., and at 27 of them the snails were found, most in the unlined irrigation canals ; in 16 of 31 unlined, but in 3 only of lined canals. In these three there was much vegetation, so that the water-flow was obstructed. Where the flow was good and the canal kept clean the snails found no chance to develop. Only 1,175 specimens of the mollusc were collected altogether—a very small number—and in 3 only of the 27 samples were they found to be infested with cercariae of *S. mansoni*. These cercariae remain infective for some time, because persons living 2½ kilometres below the place where the snails existed were infected. One place heavily infested was a tank supplied with well water ; the snails probably gained entrance to the tank by plants carried there, or by birds, or in the material used for its construction. From the tank the canals became infested and, to eradicate the vector, it will be necessary to empty out all or nearly all the water, paint the whole of the inside with strong milk of lime and wash it well with a strong jet of water. A series of photographs shows some of the poorer dwellings, the district, canals lined and unlined. *H. Harold Scott*

JAFFÉ, R., MAYER, M. & PIFANO C., F. Estudios biologicos y anatomopatologicos en animales infectados con un solo sexo de *Schistosoma mansoni*. [**Biological and Pathological Studies in Animals infested with Male** *Schistosoma mansoni*.] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Feb., v. 10, No. 1, 95–107. English summary.

Faust in 1927 stated that in snails collected in China in the dry season he found only male worms and he concluded that female worms were less resistant to inimical circumstances. In Caracas where a certain degree of moisture is maintained in the dry season by irrigation, no such preponderance of sex was observed. According to Girges, Egyptian splenomegaly results from infestation by male worms. This the present authors could not confirm. Using guineapigs, rats and rabbits, they found a large spleen in a rat infested with female worms only, and in a guineapig with male infestation only ; yet again other animals heavily infested with both male and female might have normal spleens.

The pathological lesions of necrosis and pigmentation in the liver, the spleen, intramuscular infiltrations, endarteritis, peri-arteritis and phlebitis, were the same in those infested with male worms only and in those infested with worms of both sexes. In fact, of 30 animals infested by worms of one sex only (males), 8 showed necrosis of the liver, whereas 9 out of 78 of those infested with both males and females showed this lesion. If one can draw any inference from so small a number, it would seem that male worms are more likely to cause the necrosis ; at all events the lesion cannot be ascribed to the presence of ova, but are due to toxins secreted by worms of either sex.

H. Harold Scott

MAYER, M., LUTTERMOSER, G. W. & PIFANO C., F. Investigaciones diagnosticas sobre la Schistosomiasis Mansoni en la ciudad de Maracay y Alrededores inmediatos (Estado Aragua). [**Study of Infestation by *Schistosoma mansoni* in Maracay and its Immediate Neighbourhood.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Feb., v. 10, No. 1, 165–74, 1 fig. English summary.

The following means of diagnosis of schistosomiasis in the Maracay district of th State of Aragua were used : (1) History, including age, place of residence, contact with infested water (river, irrigation canals, wells) ; (2) Clinical examination and measurement of liver and spleen ; (3) Examination of faeces ; (4) Intradermo-reaction and, if this was negative, Fairley's complement fixation test.

The numbers examined were small but the findings are, nevertheless, of interest. Only 127 were examined, 76 of them school-children The intradermal reaction was carried out in all and in the cases of 7 suspected persons, who gave a negative to this reaction and faecal examination, the complement fixation test was made. Of the 76 children, 42 were from 6 to 10 years of age and 3 of these had ova of *S. mansoni* in their stools ; of 34 between 11 and 15 years 15 were positive. Of 60 persons living in the suburbs of the town who were examined, 17 were below 15 years of age and 11 of them were passing the ova ; 43 were over 15 years and 26 of them were passing ova ; *i.e.*, 37 out of 60. Twenty-six had enlarged spleens, but, though malaria is present, it is believed that this symptom is more often due to the helminthic infestation. In 4 only were malaria parasites seen (*P. vivax*) in whom the intradermo-reaction was negative. This reaction was positive in 13 out of 40 school-children between 6 and 10 years of age and in 15 out of 30 between 11 and 15 years. Fifty-five of the general (not school) population were tested by the skin reaction and of 7 below 5 years of age 3 were positive ; 5 out of 8 between 6 and 10 years ; 1 out of 5 between 10 and 15 years, and 26 out of 35 above that age.

H. Harold Scott

MAYER, M. & PIFANO C., F. El diagnostico de la schistosomiasis por intradermorreacciones con un antigeno preparado de vermes adultos de *Schistosoma mansoni*. (Estudio fundamentado en 5000 intradermorreacciones.) [**Diagnosis of Schistosomiasis by Intradermal Reactions.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Feb., v. 10, No. 1, 3–44, 5 figs. [25 refs.] English summary (10 lines).

This is a careful study and carried out with much attention to detail. In an introductory historical account of the intradermal reaction in *S. mansoni* infestations the authors give due credit to Hamilton FAIRLEY as the pioneer in this work. They describe in detail the method of preparing their own antigen which they call *Bilharzine*. Early attempts were made with cercariae, collecting them in large numbers, centrifuging, sedimenting and filtering, but this was hazardous through handling the cercariae ; they, therefore, devised a plan for using adult worms. They prepare their antigen as follows : At first naturally infested snails were used, as they are abundant in Distrito Federal, but later they bred them from snails infested by human faeces or the livers of experimental animals. The cercariae were allowed to penetrate guineapigs and rats whose abdomens had been shaved. The latter seemed to be the more resistant to infection and guineapigs are to be preferred. Forty days later adult worms were present in the liver and a little later still in the small vessels of the mesentery and walls of the intestine. The animals were killed and the worms obtained by macerating the liver and the mesentery in saline. A good yield would be 100 worms from a rat and 300 or more from a guineapig. The

worms were dried, pulverized and suspended in phenolized saline ; later Coca's fluid was used. This contains sodium chloride 0·5, sodium carbonate 0·05 [sodium bicarbonate 0·28 per cent. according to Stitt] and phenol 0·4 per cent. ; subsequently merthiolate 1 : 5,000 replaced the phenol. The strength of the suspension was about 500 worms in 3–4 cc. of fluid. It was placed in the ice-box for 5–6 days with frequent shaking and then centrifuged and filtered, first through paper and then through a Seitz filter. The product will keep for several months.

The reaction is graded thus : 0, where there forms a papule not more than 1 cm. in diameter, with defined edges ; ±, papule of diameter 1 cm., with irregular edge ; +, papule 1–1·5 cm., edges irregular ; ++, 1·5–2 cm. papule, edges irregular or with pseudopods ; +++, 2·5–3 cm., similar in appearance. These are illustrated by diagrams and photographs.

Results.—Positive in 163 out of 171 patients, 95·3 per cent. Of 253 controls not one was positive. Helminthiasis being common in Venezuela, the test was carried out on patients with cestodes and nematodes, but the results were negative. On infestation with other trematodes, such as *Fasciola hepatica*, a report will be issued later.

The test was made on 4,045 unselected persons and 1,360 (33·6 per cent.) were positive ; 139 others (3·4) were doubtful. The positive figure is also the average of inhabitants of Caracas and its environs who harbour *S. mansoni*. A positive reaction may appear at any time from 18 to 35 days after infestation. Since the reaction persists for some long time, even more than a year, it is merely a proof of present or past infestation. Most of those reacting were between 20 and 40 years old.

Other tests were made with antigens similarly prepared, but with male and female worms separately. According to a protocol in the paper, 37 persons were tested with all three antigens, male, female and both ; the results of the two former were not very discordant, but the " male " antigen was a little better than the " female " ; the bisexual was much the best of all. Another antigen used was one prepared from a liver with abundant eggs of *S. mansoni* ; part was treated with ether, part was not. The ether-treated antigen was rather the better, but the *Bilharzine* of the authors proved by far the best of all. Another was made from an infected spleen, but it was not of much value.

H. Harold Scott

MAYER, M. & PIFANO C., F. La reacción de desviación del complemento, segun Fairley, en la Schistosomiasis Mansoni. Estudio fundamentado en 1932 reacciones. [**Complement Deviation in Schistosomiasis mansoni.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1945, Feb., v. 10, No. 1, 65–93. [25 refs.] English summary.

This is a study of Fairley's complement fixation reaction and the authors' confirmation of its use and of methods derived from it, comparing his (Fairley's) antigen from *S. spindale* with that prepared from the hepato-pancreas of *Australorbis glabratus* infested with cercariae of *S. spindale* and other cercariae and also of uninfested snails. Those interested should consult the original, for the paper is too full and congested for abstract and comprises a dozen protocols. The results may be epitomized by saying that among 238 persons proved to be infested by demonstration of ova in the faeces, 217 (91 per cent.) were positive ; whereas among 120 from non-bilharzial districts and 300 suffering from other diseases such as malaria, ankylostomiasis, amoebiasis, cancer of the liver, cutaneous leishmaniasis, etc., none was positive. After a course of tartar emetic, 5 per cent. of the positive reactors became negative, and after a second course 32 per cent. were negative. The authors conclude : " A positive test

does not signify that living worms are present at the time of examination. It is for the physician to decide whether or not the clinical symptoms presented demand treatment." *H. Harold Scott*

OTTOLINA, C. & ATENCIO M., H. Nuevos caminos para el diagnostico clinico preciso de la Schistosomiasis Mansoni. [**New Methods for the Accurate Diagnosis of Schistosomiasis mansoni.**] *Rev. Sanidad y Asistencia Social.* Caracas, 1945, Feb., v. 10, No. 1, 185–215, 2 figs. [Bibliography.]

The new methods described and evaluated are two : liver and rectal biopsy. Faecal examination for ova often fails and ova have been found for the first time after as many as 20 examinations. The complement fixation method of Fairley is not specific in that it is given also by the Fasciolidae. Yet again, as is well known, infestation may persist after apparent clinical cure.

Liver puncture is described in minute detail, for which those interested should consult the original, if they are not already *au fait* with the procedure. The material obtained is digested in 4 per cent. potash, after which the ova are easily found. It is known, however, that the female worms oviposit preferably in the inferior mesenteric veins and the eggs are found in the rectal walls, and the recto-sigmoidal region or the upper part of the rectal ampulla is usually particularly rich in ova. Again, the procedure for obtaining biopsy specimens from this site are detailed and illustrated. The ova may be seen in these specimens even when the liver biopsy proves negative, but in none of the authors' cases did the reversé obtain, the rectal biopsy was always positive if the liver had shown ova.

A table gives details of 12 patients ; 8 had had no treatment and all were positive ; one had received two courses and, with brief negative intervals, was again shown to be positive by rectal biopsy. Three had been treated and were regarded as clinically cured ; nevertheless in only one was the cure confirmed by rectal biopsy ; both the others showed ova to be present, in one there were 27, in the other 38 in a single preparation. *H. Harold Scott*

DA SILVA, L. C. T. **Splenectomy in Schistosomiasis mansoni.** *Puerto Rico J. Pub. Health & Trop. Med.* 1948, Sept., v. 24, No. 1, 69–89, 7 figs. [Refs. in footnotes.] [Spanish version 90–103.]

In the agricultural regions of Pernambuco, Brazil, it is estimated that from 36 to 50 per cent. of the population suffer from infestation by *Schistosoma mansoni*. The number of patients with parasitic splenomegaly seen in the hospitals is increasing, though the diagnosis is not easily established, owing to the infrequency with which the schistosomes or their eggs are found in the parenchyma of the spleen. Sixty patients with splenomegaly were operated upon by the author during 6½ years. Examination of the faeces for schistosome ova was positive in 54 and in the remaining 6 the diagnosis was established by liver biopsy in 4 and by subsequent post-mortem examination in 2. The ages of the patients ranged from 10 to 44 years, with maximum incidence at ages 15–24. Ascites was present in 15 patients. The most frequent symptoms were diarrhoea in 74 per cent. general weakness in 76 per cent., fever in 67 per cent. and epistaxis in 64·7 per cent. Haematemesis, due to rupture of oesophageal varices, occurred in 56·6 per cent. The Wassermann reaction was tested in 31 patients and proved to be positive in 14 ; this test may be strongly positive in *Schistosoma mansoni* infestations, even in the absence of syphilis [but no evidence is given to support this statement]. Splenectomy is indicated for the relief of portal tension and abdominal distension and for correcting leucopenia ; repeated attacks of haematemesis constitute an urgent indication for operation.

Treatment of anaemia and helminth infestations precedes operation, but the author does not give a pre-operative course of antimony, as he considers that in heavy infections it undermines the patient's resistance, which needs to be high to withstand the operation ; a course is, however, given after operation.

High spinal anaesthesia was used except in emergency operations, for which general anaesthesia was preferred. A left mid-rectus incision with careful separation of all adhesions before ligation of the pedicle was the usual method of approach, but for very large spleens a thoraco-abdominal incision was found to give better access. Post-operative haemorrhage from small vessels at the back of the stomach and spleen is a very real danger to be guarded against by careful haemostasis. Blood transfusion was only exceptionally given. There were 15 post-operative deaths in the series of 60 cases, from internal haemorrhage, haematemesis from oesophageal varices or from pulmonary complications. The best results were in young patients without cirrhosis or ascites and with over 3 million erythrocytes per cmm. and Hb. of 60 per cent. or more.

In a table a summary of the blood changes in 9 patients at intervals of one to 24 months after operation is given and compared with the condition on admission ; all show improvement in both red and white cell counts.

W. L. Harnett

Mazzotti, L. Aplicación de la intradermorreacción en casos humanos de infección por *Fasciola hepatica*. [**The Intradermal Reaction in Human Infections by** *Fasciola hepatica*.] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, Dec., v. 9, No. 4, 257–61.

The intradermal reaction with *Fasciola* antigen, used in three patients infected with *Fasciola hepatica*, gave frank positive results. The author in 1942 has already reported on equally satisfactory results with the same method in another human case.

H. J. O'D. Burke-Gaffney

Chance, M. R. A. & Mansour, T. E. **A Kymographic Study of the Action of Drugs on the Liver Fluke** (*Fasciola hepatica*). *Brit. J. Pharmacol. & Chemotherapy*. 1949, Mar., v. 4, No. 1, 7–13, 4 figs. [10 refs.]

" 1. It is possible to obtain rhythmical kymographic records from fresh bovine flukes suspended in Ringer's solution at a *p*H range from 6·5–8·5. These movements are maintained for a period of at least 2 hours and frequently as long as 6 hours.

" 2. The effect of known anthelmintics and of a number of other drugs, particularly those affecting the neuromuscular mechanism of vertebrates, have been tested on this preparation by allowing them to act for a maximum period of 45 min.

" 3. At the end of this period the addition of amphetamine restores rhythmical activity provided the drug has had only a paralysant action on the fluke. In this way it has been possible to distinguish between stimulant, paralysant, and lethal drugs.

" 4. It is suggested that the possible reason why the chlorinated hydrocarbons are so effective as anthelmintics against *Fasciola hepatica* is that they combine the stimulant action at low with the lethal at higher concentrations. A number of other anthelmintics have been shown to have other types of combined action.

" 5. Comparison with the similar test on *Ascaris* segments (Baldwin, 1943) reveals that the liver fluke as a representative of the platyhelminthes is sensitive to all the drugs which affect *Ascaris* and in addition to umbelliferone, pelletierine, extract filix mas., and gentian violet. The significance of this comparison is discussed."

HARANT, H., LAPEYSSONNIE, L. & LANCIEN. Sparganose kystique chez un noir du Gabon. [**Cystic Sparganosis in an African from Gabon.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 11/12, 666–7.

An African patient from Gabon, French Equatorial Africa, was admitted to hospital in June, 1948, with a cystic tumour in the right lumbar region accompanied by pain on moving or bending the trunk, which had begun in 1943. The tumour, situated latero-vertebrally, was hard, about the size of a nut, and painful on pressure. Fluid could not be aspirated from it. There was an eosinophilia of 24 per cent. ; the Casoni test was negative ; faecal examination showed *Strongyloides*. The cyst was removed from the subcutaneous tissue under a local anaesthetic and on being opened revealed a flat worm 4 cm. long which moved like a *Taenia* proglottis.

The authors comment on the geographical distribution and host localization of sparganosis generally and the difficulties connected with the accurate identification of plerocercoids, of which the present instance is an example.

J. J. C. Buckley

DOLD, H. & THEMME, H. Ueber die Möglichkeit der Uebertragung der Askaridiasis durch Papiergeld. [**The Possibility of Transmission of *Ascaris* by Paper Money.**] *Deut. med. Woch.* 1949, Apr. 1, v. 74, No. 13, 409.

The authors state the common methods of acquiring *Ascaris* infestation by eating raw or inadequately cooked fruits and vegetables which have been fertilized by human excreta. They then recall the work of DOLD and CHEN YÜ HSIANG of 30 years ago when they showed that typhoid, paratyphoid, dysentery, cholera and diphtheria organisms might cling to paper money and remain viable for a time. They wondered whether the ova of *Ascaris* might not similarly remain viable and be transmitted. They, therefore, tested whether ripe *Ascaris* ova on the fingers could be transferred to notes and *vice versa*, and next determined that these ova would live in an atmosphere of 50 per cent. moisture at 18°C. for some 5 weeks. Now, the average humidity in Germany in the middle of the year is 70–80 per cent. [say the authors] and the temperature for development of the ova is 15°C. Paper money is usually carried in a trouser pocket or a coat pocket where the temperature is above 15°C. They took 20 old Reichsmark notes, much used and " correspondingly dirty ", washed them in 40 cc. of filtered and sterile physiological saline and the fluid was then centrifuged at a low speed for 5 minutes ; in the deposit were found fertilized *Ascaris* ova.

H. Harold Scott

DA SILVA, L. S. **Ascariasis and its Dangers.** *Med. J. Malaya.* 1948, Sept., v. 3, No. 1, 41–8.

In the General Hospital, Singapore, approximately 25 per cent. of the children admitted are infected with *Ascaris lumbricoides*. During three years (1939–41) the author performed 1,350 autopsies on children and he claims that no less than 73 of these children died of ascariasis.

This paper consists mainly of a tabulated record of these 73 cases. They include 14 cases of acute abdominal complications ; there were seven cases of hepatic abscess, with lung abscesses in three of them, suppurative cholangitis with peritonitis in five cases, intestinal obstruction by a ball of roundworms, a perforated ulcer of the ileum, each in one case ; there was also a case of otitis media with a worm in the Eustachian tube. Roundworms were present in the abscesses in all these cases.

The clinical picture of the less dramatic cases was that of secondary anaemia, followed by enteritis and often terminal pneumonia.

L. E. Napier

WILLIAMS, W. J., SCHELLING, V. & HARTMAN, F. W. **Action of some Alkylhydroxybenzenes on Pig Ascaris** *in vitro*. *Amer. J. Trop. Med.* 1949, Mar., v. 29, No. 2, 241–5, 2 figs.

"Several new substituted alkylhydroxybenzenes have been tested for their ascaricidal properties, both by the variable exposure method and the kymograph method.

"One of these, 2-ethyl-4-chloro-6-hexylresorcinol, seems to be more active than hexylresorcinol *in vitro*."

MALDONADO, J. F., HERNÁNDEZ MORALES, F., FOX, I. & THILLET, C. J. **The Incidence of Filariasis** *bancrofti* **in Government Institutions for Children in Puerto Rico.** *Puerto Rico J. Pub. Health & Trop. Med.* 1948, Dec., v. 24, No. 2, 121–34. [Spanish version 135–49.]

A survey of the incidence of filariasis in three institutions for children in Porto Rico revealed, by microfilarial examination, percentage infection rates of 3·8, 1·3 and 10·4, respectively. In the last group clinical evidence of the infection was slight. Examination of 693 mosquitoes collected in the building housing this group showed 14·7 per cent. of them to be infected. (Details of these are tabulated.)

Of the mosquitoes collected from the three institutions 95 per cent. were *Culex quinquefasciatus* [*C. fatigans*]. *Aëdes solicitans* and *Aëdes aegypti* were infrequent and were never found to be infected. The mosquito survey indicated that although transmission of the parasite to the vector was occurring intensively, transmission from vector to human beings was more difficult.

J. J. C. Buckley

KERSHAW, W. E., with a statistical analysis by R. L. PLACKETT. **Observations on** *Litomosoides carinii* **(Travassos, 1919) Chandler, 1931. I. The Development of the First-Stage Larva.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 377–99, 7 figs. on pl. & 5 text figs. [26 refs.]

From the aspect of experimental chemotherapy against filariasis in cotton rats, a complete knowledge of the normal behaviour and appearance of the microfilaria in all phases of its existence is very desirable. The present study was designed to fill a gap in the knowledge of the early development and morphology of the larvae of *L. carinii*, from the time of birth to the appearance in the peripheral blood. Measurements and observations were made on the larvae in three different stages, those just emerged from the maternal body, those from the pleural spaces of the host, and those from the peripheral blood.

The mean lengths of larvae, numbering 200, 220 and 80, respectively, from three female worms, were respectively 68·58μ, 66·7636μ and 64·525μ. The mean length of 500 larvae from the pleura was 71·694μ and that of 500 larvae from peripheral blood was 77·932μ. There is thus an increase in length during the period of migration from the parent worm to the blood during which there is also an increase in nuclear complexity. Of special interest, however, is the shedding of a sheath—the stretched out vitelline membrane—at birth and the subsequent development of a true larval sheath during the sojourn in the peripheral blood. This is discarded in the gut of the insect vector when the larvae are ingested.

[In the light of these observations, it should be necessary now to reconsider the nature and origin of the sheath in such forms as *Mf. bancrofti* which was considered by early investigators, and hitherto accepted by many, not to be a true larval sheath, but merely an enclosing membrane derived from the egg shell or vitelline membrane.] *J. J. C. Buckley*

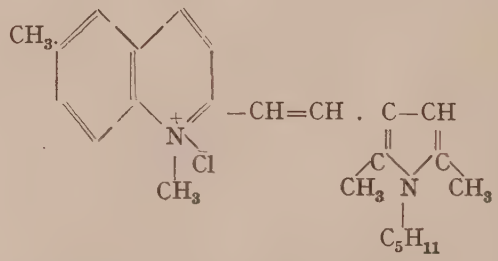
BUEDING, E. **Studies on the Metabolism of the Filarial Worm,** *Litomosoides carinii*. *J. Exper. Med.* 1949, Jan. 1, v. 89, No. 1, 107–30, 2 figs. [46 refs.]

This investigation on the filarial worm *L. carinii*, a natural parasite of the cotton rat, was undertaken to gain a better understanding of the mode of action of filaricides and hereby to aid in the selection of new therapeutic agents. For metabolic studies the worms were obtained from the pleural cavity of naturally infected cotton rats and were washed and maintained in a medium containing Na, K, Ca and Mg chlorides, to which was added a sodium phosphat buffer of *p*H 7·6. The metabolism and motility of the filariae were influenced by the nature and concentration of the metallic ions present in the medium as well as by its *p*H value. For respiration experiments, 15 to 25 mgm. of worms in 0·8 ml. of the above medium were used in a conventional Warburg apparatus at 37·5°C., with cups of 4 to 5 ml. volume. The acids produced we e determined before and after incubation, as were also total carbohydrate and glycogen. It was found that the rate of oxygen uptake of the worms was increased in presence of glucose and remained constant over a period of at least 7 hours, during which time motility was preserved. Fructose and mannose acted like glucose whereas other common substrates including lactate and pyruvate did not. After a period of anaerobiosis, during which glucose was used up, oxygen uptake was not increased and in this respect *L. carinii* differs from other helminths. Aerobically the glucose was converted to lactic and acetic acid and glycogen was synthesized. A polysaccharide other than glycogen was also present in the worms. During anaerobic incubation in presence of glucose, the polysaccharide content of the worms decreased and lactic acid was predominantly formed along with a small amount of acetic acid. Aerobically, lactate and pyruvate were utilized to a smaller extent than glucose. Respiration and metabolism were influenced to a considerable extent by fluoroacetate, iodoacetate, p-chloromercuric benzoate, cyanide and certain cyanine dyes. The latter group of substances have been shown by WELCH *et al.* [this *Bulletin*, 1947, v. 44, 1015] and by PETERS *et al.* [below], to be effective chemotherapeutic agents in cotton rat infections with this parasite. The present author found that two substances (Chemotherapy Centre Nos. 348 and 863) were effective inhibitors at low concentrations and decreased the oxidative metabolism which is apparently essential for the survival of *L. carinii*. Similar changes were noted in worms from cotton rats themselves treated with these substances. The chemotherapeutic action of the cyanine dyes in filariasis of cotton rats appears to depend upon their inhibitory effect on the respiratory metabolism of filariae. *J. D. Fulton*

PETERS, L., BUEDING, E., VALK, A. D., Jr., HIGASHI, A. & WELCH, A. D. **The Antifilarial Action of Cyanine Dyes. I. The Relative Antifilarial Activity of a Series of Cyanine Dyes against** *Litomosoides carinii*, **in Vitro and in the Cotton Rat.** *J. Pharm. & Exper. Therap.* 1949, Feb., v. 95, No. 2, 212–39. [16 refs.]

The *in vitro* and *in vivo* action of certain cyanine dyes against the filarial worm *Litomosoides carinii* of the cotton rat has been reported by WELCH *et al.* [this *Bulletin*, 1947, v. 44, 1015], and by BUEDING and also PETERS (*Ann. New York Acad. Sci.* 1948, v. 50, 115, 117). The activity appeared to be specific for that filarial species. CULBERTSON *et al.* [this *Bulletin*, 1944, v. 41, 772; 1945, v. 42, 136] and other authors have used antimony compounds to treat this infection with some degree of success. In the present investigation a search has been made for filaricides, of non-metallic type, with activity against adult worms. Cotton rats naturally infected with *L. carinii* used in screening

tests were treated intraperitoneally with an amount of drug approaching the maximum tolerated every 8 hours up to a total of 18 doses, in order to detect activity. The animals were killed 40 hours or longer after the last dose, and adult worms, when present in the pleural cavity, were removed to nutrient medium and observed at the same time as those from untreated cotton rats. [KERSHAW & BERTRAM (this *Bulletin*, 1949, v. 46, 69) have pointed out that results, obtained with wild cotton rats infected for an unknown period of time, must be interpreted with care]. The first compound to show marked activity was a member of the group of cyanine dyes—(1-amyl-2, 5-dimethy-3-pyrrole) (1, 6-dimethyl-2-quinoline)



dimethincyanin chloride, which as a class possess tertiary and quaternary nitrogen atoms separated by a conjugated chain of C atoms (*i.e.*, with alternating single and double bonds). This substance, alloted the number 348, was very active and killed all adult worms either after repeated well-tolerated doses or after a single dose near the maximum tolerated. With the antimony compounds Neostibosan and Anthiomaline, on the other hand, a cure could not be obtained. This substance 348 reduced the motility of adult *L. carinii* at a dilution of 1/1 million and affected their oxidative metabolism at a dilution of 1/40 million. Decrease in the respiration of mammalian tissues was affected only by a concentration 1,000 to 2,000 times as great. Cyanine dyes in general appeared to exert their effect through action on oxidative enzymes. All the drugs which were active *in vivo* were also active *in vitro*, but the reverse was not true. BUEDING [above] has made an extensive study of the respiratory metabolism of filarial parasites, and his *in vitro* methods were used as an aid in screening new compounds. Many substances based on the model of 348 above and others of widely different constitution were studied as well as non-cyanine dyes with structural features similar to cyanines. None of the latter was active *in vivo* but some showed activity *in vitro*. The data given must be studied in the original. The authors consider that any substance active against filariasis in man would show both *in vivo* and *in vitro* activity against *L. carinii*. On that basis a number of substances have been selected for further study with a view to trial in the human disease. *J. D. Fulton*

VARGAS, L. Notas sobre la oncocerciasis. VII. Infección experimental de *Simulium* (*Lanea*) *mangabeirai* con *Onchocerca volvulus*. [**Notes on Onchocerciasis. VII. Experimental Infection of** *Simulium* (*Lanea*) *mangabeirai* **with** *Onchocerca volvulus*.] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, Dec., v. 9, No. 4, 309–11.

The English summary appended to the paper is as follows :—

" A *Simulium* (*Lanea*) *mangabeirai* female, obtained by culture of a collect made in the town of Los Remedios, Méx., at 2,645 mts. above the sea level, bit

in the Laboratory of Mexico City a carrier of *Onchocerca volvulus* microfilariae ; 124 hours after the infective meal the simulium showed sausage forms developing in the muscles of the thorax."

HITCHCOCK, Dorothy J. **Artifacts in Transparent Adhesive Tapes used for Perianal Pinworm Swabs.** *Amer. J. Trop. Med.* 1949, Mar., v. 29, No. 2, 247–8, 2 figs.

" A microscopical study was made of two brands of transparent adhesive tapes for artifacts resembling *Enterobius vermicularis* eggs. Very few artifacts, other than bubbles, simulating pinworm eggs were found."

BOYCOTT, J. A. **An Improved Swab for the Detection of Threadworm Ova.** *J. Clin. Path.* 1949, May, v. 2, No. 2, 149.

The author describes a device for the detection of ova of *Enterobius vermicularis* which has been found to have some advantages over N.I.H. swabs [this *Bulletin*, 1937, v. 34, 878].

It consists of a wooden tongue depressor (6 in. × ¾ in.) over the end of which is doubled a strip of Cellophane (3 in. × 1 in.) held in place by several turns of a rubber band.

The swab is rubbed along the peri-anal folds, preferably as soon as the patient awakes in the morning : the pressure used should be just short of causing pain.

The swab is placed in a paper envelope (about 2 in. × 4 in.), bearing the patient's name. In the laboratory, the Cellophane is opened out and attached to a slide by means of a drop of Canada balsam. The areas showing epithelial and faecal débris are picked out microscopically with a ⅔ in. lens.

The single crease in the Cellophane, the strength and the simple packing are improvements on the original N.I.H. swab. *H. J. O'D. Burke-Gaffney*

HAND, E. A. & CRISWELL, R. H. **Otitis Externa due to** *Oxyuris vermicularis*. *Arch. Dermat. & Syph.* 1949, Feb., v. 59, No. 2, 249–50.

The authors discuss some of the literature relating to external otitis and conclude that the rôle of fungi in the causation of this condition has been greatly overstressed. Injudicious or excessive topical treatment of seborrhoeal, eczematous and related affections of the external auditory canal is a common cause of otitis externa and picking and scratching of the ears is a frequent habit in those affected.

Enterobius vermicularis may be found occasionally in the nose and ears of persons in the tropics, infection being presumably carried by the nails. The present case refers to such an infection. It relates to an ex-officer of the U.S. Army who complained of pruritus and discharge from both ears. This had been noticed first in Burma some months previously. The patient had had no treatment and no history of previous ear affections or of pruritus ani.

On examination, the ear drums were intact and hearing was normal. There was scaling and erythema around the external auditory meatus and up the canals. In a slight sero-ceruminous discharge from the ears, microscopical examination revealed many motile threadlike worms which were determined to be " a genus [*sic.*] of Ox. vermicularis ". No ova were found in the discharge, under the nails or around the anus. No adult worms were found in the stool.

The condition cleared up on cleaning of the ears with alcohol and the application of a few drops of 20 per cent. benzyl benzoate in calamine lotion twice daily for two weeks. *H. J. O'D. Burke-Gaffney*

ERHARDT, A. Einige grundsätzliche Bermerkungen zur Wirkung von Oxyurenmitteln. [**Fundamental Points on Measures for dealing with Enterobiasis.**] *Deut. med. Woch.* 1949, Apr. 1, v. 74, No. 13, 406–7.

This is a contribution to Professor Rodenwaldt's 70th Birthday Festschrift. The author divides his subject into (i) aetiological action, *i.e.*, drug treatment of the infesting worm ; (ii) prophylaxis. Under the first he mentions in particular oil of chenopodium, but notes that it is not sufficient merely to examine the faeces soon after and, finding no ova, to report the patient as cured. The worms may remain unexpelled for some time and search must be assiduously carried out for 4–5 weeks to prove death of the worms and even longer (up to 3 months) before one can be certain that all have been expelled. They may have lodged in the appendix and the drug may not have reached them in their hiding-place.

As for prophylaxis, we must guard against auto-infection *per os*, and also by inhalation of ova in dust. Treatment of the patients and so drying up the source of supply, as it were, and local application of some ointment to ease the itching and prevent infection of the fingers are obvious means for attaining this end. *H. Harold Scott*

CARTER, J. R. **Plasma Cell Hyperplasia and Hyperglobulinemia in Trichinosis. The Duration of Larviposition.** *Amer. J. Path.* 1949, Mar., v. 25, No. 2, 309–23, 6 figs. on pl. [30 refs.]

" Viable adult trichinae, including gravid females, were observed microscopically in the small intestine of a fatal case of human trichinosis 115 days after the onset of symptoms. The patient was continuously hospitalized and under close observation for 87 days. Reinfection, although remotely possible, was considered to be adequately excluded. The period of persistence of living adult trichinae in the human intestine is the longest thus far recorded. The continued release of larvae over relatively long periods of time is of considerable significance from a clinical, prognostic, and therapeutic point of view. The degree of infection as determined by counts with the trichinoscope was considered moderate to heavy.

" The diffuse plasmacytosis with associated hyperglobulinemia is considered to constitute an unusual, if not unique, cellular response to trichinosis."

DEFICIENCY DISEASES

KRUSE, H. D. **A Concept of the Etiological Complex of Deficiency States with especial consideration of Conditions.** *Milbank Memorial Fund Quarterly.* 1949, Jan., v. 27, No. 1, 5–97, 3 figs. [48 refs.]

In this comprehensive examination of the aetiology of deficiency states, the author emphasizes that nutritional deficiency is not necessarily synonymous with dietary deficiency. In the past much emphasis has been laid upon the relationship of diet to disease, to the exclusion of sufficient consideration of all the other environmental conditions, both internal and external, which govern the adequacy of nutrition at a cell level.

Many external environmental factors, socio-economic, physical, and chemical, in addition to simple dietary intake, affect the adequacy of tissue nutrition ; and the internal environment may affect this adequacy through impairment of many metabolic channels, and changes in many functions and reactions. As the author summarizes his able essay " the possibility that a disease of

unknown cause may be nutritional in nature is not to be forthwith dismissed because it apparently is not the effect of dietary deficiency alone ; rather, this contingency can be examined on broader aetiological grounds ".

Dean A. Smith

CORKILL, N. L. **Dietary Change in a Sudan Village following Locust Visitation.** *Africa.* 1949, Jan., v. 19, No. 1, 1–12, 5 figs. on 4 pls. & 1 map. [18 refs.]

The population of the Fung area of the Anglo-Egyptian Sudan normally cultivate millet, cow-peas and sesame seed as subsistence crops, and they barter animals and milk products with cattle-owning nomads. In addition they have a number of valuable wild fruits at their disposal, and consume a considerable proportion of their millet fermented as beer. Their diet, as assessed in a series of seasonal surveys, in normal years, is entirely adequate by any standards.

In 1938 their crops were destroyed by locusts to a very great extent, and for the ensuing 8 months they were very short of their normal foods and used bush products increasingly. The main foods upon which they depended were guinea-fowl, gingerbread nut (*Hyphaene thebaica*), the desert date (*Balanites aegyptiaca*) and the cluster yam (*Dioscorea dumetorum*). Evaluation of this partial famine diet indicated a small, possibly unimportant, deficiency in total calories, an almost adequate intake of fat, salt, nicotinic acid and ascorbic acid, but important deficiency of vitamins A, B_1 and riboflavin.

It was possible to carry out a clinical examination of the community in the famine area after 4 months of famine and after 8 months, at which time the Government stepped in with famine relief measures. After 4 months there was no evidence of major deficiency disease, but after 8 months all complained of pain in the belly and a sense of distension. These signs and symptoms suggest either poisoning from desert dates and dioscorine or vitamin B_1 deficiency, or possibly both. One case only showed neurological manifestations characteristic of dry beriberi, and this, taken with the prevalence of digestive disturbance, abdominal distention and the presence of a buccal frieze, was considered to suggest that the population was on the brink of an outbreak of dry beriberi. [Some workers would not agree with the author's interpretation of buccal frieze as suggestive of beriberi.]

It is concluded from this most interesting series of observations that much can be done to insure against nutritional catastrophe from locust visitations, by growing a reserve root crop such as manioc, and by growing ground nuts.

Dean A. Smith

SING, K. G. **Nutritional Survey in Gandhi Nagar Camp, Jullundur.** *J. Indian Med. Ass.* 1949, Jan., v. 18, No. 4, 96–9.

A clinical nutritional survey was carried out upon 6,000 refugees from Western Pakistan ; evidence of frank deficiency was found in 8·3 per cent. Enquiry indicated that the diets of these refugees had, at their homes, been satisfactory and that deficiency had only arisen in transit. Incidence was higher in adults than in children and in men than in women. The outstanding manifestations were those of deficiency of B complex factors, especially riboflavin, though cases of vitamin A deficiency and scurvy were seen.

Treatment of established cases with vitamin preparations was generally rapid and successful : strong recommendations are put forward for improving the camp diet, including the use of germinated beans, nuts, vegetables, eggs and liver.

Dean A. Smith

THOMSON, F. A. **Dietary Deficiencies in Children in the Island of Viti Levu, Fiji.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 487–92, 8 figs. on 4 pls. [21 refs.]

In the Island of Viti Levu, Fiji, urbanization is rapidly spreading, and there is a change from the traditional diet to a preference for sophisticated foods and tinned store-goods. White bread, sweet tea and large quantities of sugar are becoming the staple diet of most of the smaller children from weaning time.

A clinical survey of over 7,000 school and pre-school children, carried out in 1947, has shown the effect of this change on the physical status of the children.

There was found no evidence of real starvation, the diet being apparently sufficient in calories, but there was evidence of deficiency of protein, vitamin A, factors of the B complex and, seasonally, of vitamin C. The most marked changes were found in the teeth, and it was in the 5 to 8 years age group that the highest proportion (65 per cent.) of children showed these changes.

The earliest changes seen were defects of enamel with roughening and pitting, which appeared to advance, with discolouration, to frank caries.

The changes attributable to vitamin A deficiency, mainly phrynoderma and xerophthalmia with Bitôt's spots, responded well to treatment with cod liver oil, and the scorbutic gums disappeared in the fruit season. Xerosis of the skin was very common.

A serious aspect of the deficiencies discovered, though some of them are themselves of comparatively little consequence, is that they indicate a rapidly deteriorating diet in an area where good food is readily obtainable, particularly fish and fruit, and that they are undoubtedly associated with less evident and possibly irreversible changes and with lowered resistance to other diseases.

It is interesting to note that Gilbertese children, whose traditional staple diet of coconuts and fish had not suffered changes of sophistication, showed none of the effects recorded on Viti Levu.

[There is a minor confusion of terminology. The term *cheilosis* is usually now restricted to lesions of the vermilion of the lips, and the term *perlèche* is used to describe the lesions at the angles of the mouth, synonymous with *angular stomatitis*.] *Dean A. Smith*

TROWELL, H. C. **Malignant Malnutrition (Kwashiorkor).** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1949, Mar., v. 42, No. 5, 417–33, 6 figs. [Numerous refs.] Discussion 433–42 [HIMSWORTH; WATERLOW; MCROBERT, G.; MCKENZIE, A.; CHESTERMAN, C. C.; SMITH, D.; BENNET, J.; NAPIER, L. E.; EARLY, E. P. M. N.; HARE, K. P.; TROWELL (in reply)].

Kwashiorkor has now been reported from many parts of the tropical and sub-tropical world, and there are indications of its occurrence in Southern Europe. It goes under many names and its presenting clinical features vary, but workers are increasingly in agreement that the essential features are growth failure, oedema, fatty liver and lowered plasma albumin, while commonly associated deficiency lesions include depigmentation of skin and hair, dermatosis, lesions of mucocutaneous junctions, and diarrhoea.

The basic aetiology is becoming more evident; the disease starts at the time of weaning, and is associated with a low protein, relatively high carbohydrate diet. Weaning on to starchy " paps ", made from a variety of cereals, with no other source of protein, is common practice in many areas. There can be little doubt that the condition is one of nutritional deficiency of tissues, but this does not necessarily imply that the defect is dietary: cases undoubtedly occur on a basis of pure dietary deficiency, but parasitic, helminthic and bacteria infections and infestations commonly accentuate or even cause the condition

The pathology of the liver was studied by biopsy in 161 cases at Mulago Hospital, Uganda, and the sequence of changes has been traced from initial fatty infiltration through periportal fibrosis to diffuse cirrhosis of the Laennec type. Atrophy and fibrosis in the pancreas, and changes in the salivary glands have also been found.

Anaemia in uncomplicated cases is usually mild in degree, and normocytic and orthochromic in type. However, when there is heavy infection with malaria or hookworm the anaemia may be severe, and constant blood destruction and attempted regeneration produce high degrees of reticulocytosis and apparent macrocytosis.

Successful treatment depends on the administration of sufficient readily-available protein, milk proving more effective than meat or liver, and the careful eradication of all infections and infestations.

The author concludes that this disease, based either on dietary imbalance, heavy parasitization or a combination of the two, affects the majority of African children in some degree, and that its results, in non-fatal cases, lead to impaired development, subnormal function, diminished resistance to intercurrent disease and premature senility and death.

[The author has devoted many years to the study of this condition and contributed greatly to our understanding of it. This authoritative and well-balanced review is important and valuable. There is a comprehensive bibliography. See also this *Bulletin*, 1948, v. 45, 633, 635, 724.]

The discussion was mainly centred on the interplay and relative importance of malnutrition and infection in the aetiology in Kwashiorkor.

WATERLOW made a valuable contribution in suggesting that organs most active in handling protein are most vulnerable to protein deficiency. Such organs are the intestines, pancreas and liver, and the concept of an initial defect of enzyme formation, with consequent defect of digestion and absorption, would explain much of the complex clinical picture and the difficulties of treatment.

Dean A. Smith

HARTZ, P. H. **Pancreatic Atrophy in Infants with Fatty Liver.** *Documenta Neerlandica et Indonesica de Morbis Tropicis.* Amsterdam. 1949, Mar., v. 1, No. 1, 41–9, 6 figs. [15 refs.]

In the disease of infants and young children now widely recognized and known as kwashiorkor or malignant malnutrition, and characterized by liver damage, hypoproteinaemia and anaemia, pancreatic changes have been described by several workers. DAVIES [this *Bulletin*, 1948, v. 45, 633] in Uganda found fibrosis in many and atrophy in a few cases; WATERLOW [*ibid.*, 724] in the West Indies found atrophy of acinar cells; while MAGHALHÃES CARVALHO [*ibid.*, 635] in Brazil and VÉGHELYI (*Lancet*, 1948, Mar. 27, 497) in Buda-Pest found diminution in pancreatic enzyme secretion.

Microscopic examination of the pancreas was performed on 14 infants who had died with fatty infiltration of the liver. It was possible to obtain the post-mortem material very fresh. There was advanced atrophy of the acinar cells in all cases. The islet tissue appeared normal. The fibrosis, described by Davies in older children, was not seen in these babies. In a series of controls who died of intestinal or respiratory infection, or of undernourishment without severe fatty infiltration of the liver, no such severe pancreatic atrophy was found.

Although fatty infiltration of the liver is relatively common in Curaçao (49 cases in 249 autopsies) the " fully developed syndrome of fatty liver disease " [presumably characterized by the skin, hair and muco-cutaneous-junction lesions of associated avitaminoses—though this is not stated] is rare.

The author concludes that the primary lesion of this disease is in the pancreas and that fatty infiltration of the liver is secondary to it.

[Another interpretation of such findings has been put forward and was summarized in a leading article in the *Lancet*, 1949, Jan. 29, 188. Most workers are agreed that the main aetiological factor in the disease is protein deficiency, in the presence of relative excess of carbohydrate intake. It is suggested that the organs most active in handling protein are also most vulnerable to protein deficiency : such organs are the pancreas, intestinal tract, liver and salivary glands, in all of which lesions have been described. Moreover, much of the protein utilized by the gut, pancreas and salivary glands goes into the formation of digestive enzymes, the production of which is known to be impaired in fatty liver disease. Thus it may be considered, rather than that disease in one organ is secondary to disease in another, that there is, based on deficiency of total protein or some protein components, failure of and damage to all those organs which utilize protein most rapidly. As these organs are mainly concerned with digestion and absorption, this concept would explain the complexity of the clinical picture, the readiness with which secondary deficiencies occur, the variability in the results of treatment and the tendency to the establishment of a vicious circle.] *Dean A. Smith*

SPRUE.

STEFANINI, M. **The Diagnosis and Pathogenesis of Tropical Sprue.** *Acta Med. Scandinavica.* 1949, Mar. 31, v. 133, No. 2, 113–26, 1 fig. [60 refs.]

This paper epitomizes a review of the sprue syndrome carried out in British India during the war on almost 6,000 cases of tropical sprue occurring among military units. The fundamental symptoms are represented by a particular defect of intestinal absorption which is especially detectable in the case of fats.

The progression of the case is closely related to intestinal malabsorption and can be divided into three successive stages : a first in which the initial signs of impaired intestinal absorption predominate ; a second in which secondary deficiency signs set in, and a third in which with the appearance of macrocytic anaemia, the patient presents the complete picture of tropical sprue. The first two stages include also the mild and incomplete forms of the sprue syndrome.

In the author's experience the disease was found as frequently in Indians as in Europeans.

A partial defect of intestinal absorption of fats, which is usually detected earlier and more easily than that of any other dietary constituents, represents the basis for the diagnosis. The " fat-balance " technique which the author describes probably represents the best method of study of intestinal absorption. Chemical analysis of the faeces usually shows high steatorrhoea with split/unsplit fat ratio and soaps/split fat ratio higher than normal. The greatest part of split faecal fat in sprue appears to be present as soaps. Dietary deficiencies constitute the most important factor among those leading to the development of tropical sprue, but by itself it is not sufficient to explain *all* the peculiarities of the series of cases described in India during the war such as the epidemic appearance in a particular period of the year and the sudden " explosive " high incidence among military units shortly after their transfer to special areas. It would appear that tropical sprue occurs epidemically whenever and wherever favourable seasonal, local and climatic conditions exist. *P. Manson-Bahr*

Bonnin, H. & Moretti, G. F. De l'action élective de l'acide folique dans la sprue. [**Elective Action of Folic Acid in Sprue.**] *Bull. Soc. Path. Exot.* 1949, v. 42, Nos. 3/4, 129–32.

An account of 3 cases.

HAEMATOLOGY

Wroblewski, F., Weiner, M. & Shapiro, S. **A Simplified Procedure for Blood Cell Counts and Haemoglobin Determination.** *J. Clin. Path.* 1949, May, v. 2, No. 2, 138–40.

Taylor, G. F., Chhuttani, P. N. & Kumar, S. **The Meat Ration and Blood Levels. Investigation of Indian Soldiers in Persia and Iraq, 1944.** *Brit. Med. J.* 1949, Feb. 5, 219–21.

Haematological investigations were carried out among Indian soldiers in Shaiba (Iraq) in 1944. The men were engaged on heavy pioneer work (44 hours a week) and were on Army rations of over 3,000 calories with over 80 gm. of protein. Random samples of 40 meat-eaters and 42 vegetarians were taken for the investigations. The only difference in the rations, which consisted of rice or atta, dâl, ghee, tinned milk, onions, potatoes and fresh leafy vegetables (when available), was that in the former group a ration of 6 ounces of fresh mutton (with bone=4 ounces without bone) was given on 5 days a week.

The means of the red cell counts and of the haemoglobin estimations were significantly lower among the vegetarians, $4{\cdot}67 \times 10^6$ and 14·32 gm., compared with the meat-eaters, $5{\cdot}55 \times 10^6$ and 15·44 gm. The M.C.V. was significantly higher, 109·48 c.μ. in the vegetarians than in the meat-eaters, 96·33 c.μ. The M.C.H.C. in both groups was low, 28·54 and 28·32 per cent. (indicating a common iron deficiency). Eight of the vegetarians had red cell counts below 4×10^6 and two showed marked anaemia, below 3×10^6.

The sternal marrow showed significantly higher percentages of megaloblasts, erythroblasts and macroblasts among vegetarians.

"There was no clear clinical difference between the two groups." "The vegetarians could often be distinguished by a tired look." Associated infections, malaria, bacillary dysentery and hookworm, were present in both groups. Three severely anaemic men from the vegetarian group were admitted to hospital for thorough investigation; in these no complicating infections were found, although one had recently had bacillary dysentery. On the ordinary unit diet and rest in bed, the blood pictures of two of these men returned to normal within four weeks.

The authors conclude that, since the only constant aetiological factor in the production of the defective haematological state in the vegetarians was the absence of the weekly ration of 20 ounces of mutton, under conditions of hard physical work, diet alone, unassisted by coincident infections, can produce macrocytic anaemia. *L. E. Napier*

Chhuttani, P. N. **A Report of 46 Cases of Anaemia in the Punjab with special reference to Nutritional Macrocytic and Addisonian Anaemia.** *Indian Med. Gaz.* 1948, Nov., v. 83, No. 11, 508–13. [14 refs.]

The aetiological varieties and types of anaemia encountered in a series of forty-six cases in the Punjab are recorded: in 40 of the 46 cases studied, the

anaemia was classed as dyshaemopoietic. Of these, 21 were cases of iron-deficiency anaemia and 14 deficiency of the haemopoietic principle. Of the latter, 7 were nutritional macrocytic anaemia and 2 Addison's pernicious anaemia: these last 9 cases form the material on which this paper is based.

" Two cases of nutritional macrocytic anaemia not complicated by malaria or splenomegaly had hyperbilirubinaemia comparable to that seen in Addisonian anaemia. These cases had marked anisocytosis comparable to that expected in Addisonian anaemia. This was regarded to be the possible explanation of the unusual finding of hyperbilirubinaemia.

" In these two cases the Price-Jones curves were indistinguishable from those seen in Addisonian anaemia.

" They fulfilled textbook criteria of Addisonian anaemia. Positive clinical evidence against a possible nutritional aetiology was forthcoming. Both were regarded to be instances of true Addisonian anaemia.

" Differential diagnosis of nutritional macrocytic and Addisonian anaemia is discussed and it is concluded that the absence of intrinsic factor in the gastric juice of our suspected patients must be proved before the existence of Addisonian anaemia in India can be incontrovertibly established. A simple method to carry out this proof is suggested." *L. E. Napier*

SMITH, C. H. **Detection of Mild Types of Mediterranean (Cooley's) Anemia.** *Amer. J. Dis. Children.* 1948, Apr., v. 75, No. 4, 505–27, 8 figs. (1 map). [Refs. in footnotes.]

Cooley's anaemia is confined mainly to persons of Greek, Italian (principally Sicilian), and Syrian origin, and the parents and siblings of patients with severe forms of the anaemia may show clinical and haematological evidence of the disease, varying from this trait to a moderate form of anaemia. There are over 5 million persons of these origins in the United States and a recent investigation suggested that 1 in 25 of the Italians in the city of Rochester, N.Y. had a mild form of the disease.

The present report is based upon the investigations in 47 families with Cooley's anaemia. Clinically, persons with the trait or a mild form of the disease may show none of the classical features, the facies, the skeletal changes, cardiac enlargement and murmurs, and pains in the joints, but in mild cases there may be pallor and splenomegaly.

The changes in the blood on which the diagnosis depends are as follows:—

" Blood smear and blood count show hypochromic macrocytes, basophilic stippling, oval and target cells, polycythaemia.

" Morphologic changes in erythrocytes are far in excess of the degree of anaemia.

" Resistance of the red cells to haemolysis in hypotonic solutions of sodium chloride is increased.

" Iron or other forms of antianaemia therapy fail to restore normal blood levels."

Figures are given showing the incidence in the 47 families. In 35 families both parents were examined: in every instance of a severely anaemic child, both parents had a mild form of the disease or showed the trait, and, when one parent only was examined, that parent showed the trait. In every instance where there were siblings, one or more were affected. In every instance of a mildly anaemic child or a child with the trait, at least one parent was affected, and when there were siblings at least one was affected. The first-born child most frequently escaped the disease or the trait.

Of the various names suggested the author prefers Mediterranean (Cooley's) anaemia, with the qualifications, mild, moderate or severe.

The author concludes with a plea for a more thorough investigation of the disease, and especially of mild forms, in the recognized countries of origin of this disease and in other countries from which severe cases have been reported.

L. E. Napier

London, I. M., Shemin, D., West, R. & Rittenberg, D. **Heme Synthesis and Red Blood Cell Dynamics in Normal Humans and in Subjects with Polycythemia Vera, Sickle-Cell Anemia, and Pernicious Anemia.** *J. Biol. Chem.* 1949, May, v. 179, No. 1, 463–84, 9 figs. [27 refs.]

Dickstein, B., Landmesser, W. E., Jr., Love, W. E., Wilson, T. H. & Wolman, I. J. **The Osmotic Resistance of Human Erythrocytes in Normal, Carrier and Anemic States : with special reference to Changes due to Age, Race, Sickle-Cell Anemia, Mediterranean (Cooley's) Anemia and Congenital Hemolytic Icterus.** *Amer. J. Med. Sci.* 1949, Jan., v. 217, No. 1, 53–61, 6 figs. [28 refs.]

The authors adopted a method of measuring osmotic resistance of erythrocytes which was suitable for photographic reproduction. The solutions that they used were 0·18 M glycerol in 0·36 per cent. NaCl, 0·24 M thiourea in 0·18 per cent. NaCl, 0·47 per cent. NaCl, and 0·36 per cent. NaCl. They tested the osmotic resistance in 170 normal and 90 abnormal persons.

They found that in normal white children up to 10 years of age the osmotic resistance was greater than in white adults, but that in negroes this difference did not exist. The normal resistance of the negro is greater than that of the white man. These differences make it essential that control examinations should always be made with the blood of persons of a comparable age and colour group.

In sickle-cell anaemia the osmotic resistance is higher than in the normal negro ; in the sickle-cell trait it shows an intermediate position.

In Mediterranean (Cooley's) anaemia, the osmotic resistance is greater than in the normal person ; in the carrier (person showing the trait) the erythrocytes show a slightly greater degree of resistance than in the patient with the anaemia.

In congenital haemolytic icterus a markedly lower degree of resistance is shown ; the method detects increased fragility in cases in which the ordinary methods do not.

The osmotic resistance was tested in several other anaemic states including iron-deficiency anaemia and pernicious anaemia and found to be within normal limits.

L. E. Napier

Callender, Sheila T. E., Nickel, J. F., Moore, C. V. & Powell, E. O. **Sickle Cell Disease : studied by measuring the Survival of Transfused Red Blood Cells.** *J. Lab. & Clin. Med.* 1949, Jan., v. 34, No. 1, 90–104, 8 figs. [15 refs.]

Employing the Dacie and Mollison (*Lancet*, 1943, May 1, 550) technique, the authors studied the time of survival of red cells in sickle-cell disease. Normal cells transfused into subjects with sickle-cell anaemia survived normally. Cells from patients with sickle-cell anaemia transfused into normal subjects or into another patient with sickle-cell anaemia showed a shortened average time of survival ; the curves showed a sharp fall, indicating the rapid destruction of half or more of the cells, within 10 days, followed by a slow decline to the zero line which was reached in about 60 days, indicating a much slower destruction of the remaining cells.

Cells from a healthy subject with the sickling trait transfused into normal subjects or patients with sickle-cell anaemia survived normally.

Oxygen inhalation (70–80 per cent.) slowed the rate of destruction of sickle-cell anaemia cells in one subject with sickle-cell anaemia, but not in another. The survival time of trait cells in a cyanosed boy with congenital heart disease was normal.

" The findings indicate that the defect in sickle-cell anaemia is inherent in the red blood cell. There is evidence to suggest that sickling is not, as has been thought, a function of age of the cell but that the cells in sickle-cell anaemia vary constitutionally in their liability to sickle. It is suggested that the difference between the anaemia and the trait is qualitative and not simply one of degree." *L. E. Napier*

WILLIAMS, A. W. & MACKEY, J. P. **Rapid Determination of the Sickle Cell Trait by the Use of a Reducing Agent.** *J. Clin. Path.* 1949, May, v. 2, No. 2, 141–2.

There is need for a simple and accurate technique for determining the sickle-cell trait, which will serve for rapid exclusion of sickle-cell anaemia in practice and which can be used for uniform survey work. The authors refer to the deficiencies of the sealed wet preparation and also to various improved methods : but some of the latter are complex and not suitable for the clinical side-room. In 1928, HAHN [this *Bulletin*, 1928, v. 25, 1001] and later SHERMAN (*Bull. Johns Hopkins Hosp.*, 1940, v. 67, 309) showed that sickling only occurs in those having the sickle cell trait when corpuscular haemoglobin is in a reduced or dissociated state ; the change is accelerated by a low *p*H.

The authors sought an acid reducing agent which would cause rapid dissociation of oxyhaemoglobin, and hence reveal sickling in a short time, without causing damage to the red cell in isotonic solution. Sodium hydrosulphite (dithionite, $Na_2S_2O_4$) was selected and was found to fulfil these conditions admirably.

A 2·1 per cent. aqueous solution (in freshly boiled distilled water, allowed to cool) was found to be isotonic and to have a *p*H of 6·4. Sodium hydrosulphite is a powerful reducing agent which decomposes in moist air : a solution will not keep indefinitely and the 2·1 per cent. solution is therefore made once weekly and kept in small tubes sealed with liquid paraffin. A tube should be discarded at the end of the day on which the seal has been removed.

For the test, a drop of the isotonic sodium hydrosulphite solution is taken up in a fine Pasteur pipette and about one-sixth of this quantity of blood is drawn up in apposition to it. The whole is expelled on to a clean slide and rapidly mixed : the slide is inverted on to a cover slip (which need not be sealed) and examined under the $\frac{1}{6}$ in. objective. The same pipette may be used for any number of patients, if it is rinsed in saline.

If the sickle-cell trait is present, sickling occurs in 3 to 15 minutes and rapidly becomes generalized : it usually appears earliest in cells near the edge of the coverslip. If no sickling occurs after 20 minutes, the blood may be pronounced negative for the sickle-cell trait. Sickling never occurs in normal blood (after half an hour, red cells may, however, become crenated).

This technique was compared with the wet sealed preparation (read at 48 hours) in the case of 100 African schoolboys. There was complete agreement between the methods. The new technique always gave clear results in 20 minutes, while the sealed wet preparation sometimes gave doubtful results after 24 hours. (The numerical results will be published separately as part of a survey.)

The authors consider this technique to be superior to others in current use as regards speed, simplicity and reliability.

In a footnote, reference is made to the work of THOMAS and STETSON (*Bull. Johns Hopkins Hosp.*, 1948, v. 83, 176) which was noticed by the authors since their paper was sent for publication. The authors quoted found a saturated solution of hydrogen sulphide to be the most reliable and rapid agent for demonstrating sickling, among sulphydryl compounds which they tried. The present authors believe that sodium hydrosulphite has practical advantages as to odour, stability and preparation of the solution.

H. J. O'D. Burke-Gaffney

SCOTT, R. B., CRAWFORD, R. P. & JENKINS, M. **Incidence of Sicklemia in the Newborn Negro Infant.** *Amer. J. Dis. Children.* 1948, June, v. 75, No. 6, 842–9, 1 fig.

The blood of 262 negro infants selected at random, were tested for the sickling trait by the coverslip method : one drop of blood in isotonic saline was placed under a coverslip surrounded by petrolatum and examined after 24 to 48 hours at room temperature. On the first day of life, 7, or 2·6 per cent., gave a positive result. Of the total, 133 were tested again on the third day of life of which 3, or 2·2 per cent., were positive, and 129 were tested on the fifth day of life of which 6, or 4·6 per cent., were positive. Two that gave a negative test on the first day became positive by the fifth day, so that a total of 9, or 3·4 per cent., showed the sickling trait in varying degrees. In every case a blood count showed the haemograms to be within the normal range.

Two hundred and nine older children were tested ; of these 16, or 7·6 per cent., showed the sickling trait. Blood counts were done in 7 of these children and 2 were found to be anaemic and were diagnosed as active sickle-cell anaemia.

Three children showing the trait in infancy were tested again at 7, 11 and 17 months, and in all these cases the percentage of sickling was increased, from 20, 10 and 40 to 29·2, 37·0 and 85·8 per cent., respectively. *L. E. Napier*

VENOMS AND ANTIVENENES

AHUJA, M. L. & BROOKS, A. G. **Mode of Action of Russell's Viper (Daboia) Venom.** *Indian J. Med. Res.* 1948, Apr., v. 36, No. 2, 173–80, 1 graph.

" 1. Experimental evidence strongly supports the view that daboia venom consists of only one fraction of any pathological importance, i.e. a strong blood-coagulant fraction.

" 2. Histological examination of tissues of animals dying of daboia-venom poisoning show that there is extensive deposition of fibrin in capillaries. This deprives the circulating blood of its fibrin content rendering it incoagulable. Such incoagulable blood is itself a coagulant proving that no ' anti-fibrin ferment ' exists in the venom."

GRASSET, E. **Standardization of the Cobra (*Naja flava*) Antibody. A Comparative Study by the Method of Assay at various Levels and by the Selected Antivenene Single-Level Method.** *Bull. World Health Organization.* Geneva. 1949, Mar., v. 2, No. 1, 69–83, 1 fig.

SERGENT, Et. Étude comparative du venin de scorpions mexicains et de scorpions nord-africains. [**Study comparing the Venom of Mexican Scorpions with that of North African Scorpions.**] *Arch. Inst. Pasteur d'Algérie.* 1949, Mar., v. 27, No. 1, 31–4, 1 fig.

The author's method of studying scorpion venom is probably known to readers of this *Bulletin*, but may be briefly recapitulated. The telson is removed,

dried at 37°C., and kept in the dark in a sealed tube. For testing, it is ground in a mortar and the resulting powder is macerated for several hours in 0·9 per cent. sterile saline with glass beads and repeatedly shaken. White mice are the experimental animals used and the injection is made subcutaneously. The m.l.d. for mice of 20 gm. of the venoms of the North African scorpions is :

Prionurus australis	1/20 of a telson
Prionurus amoreuxi	1/5 ,, ,, ,,
Prionurus hoggarensis	1/12 ,, ,, ,,
Buthus occitanus	½ ,, ,, ,,
Hottentota gentili	¾–1 ,, ,, ,,
Scorpio maurus	7 telsons

The first-named is, thus, much more toxic than the others.

Two Mexican scorpions, *Centruroides noxius* and *C. limpidus limpidus* have been studied in the same way. Their telsons are much smaller than that of *P. australis*, about half the length and breadth and one-third to one-fourth the weight. The fatal dose for the white mouse is in each case one telson (8 mgm.). *C. noxius* is rather the more toxic of the two ; ¼ telson (2 mgm.) kills one out of two mice, whereas with ¼ (2 mgm.) and even ½ (4 mgm.) of *C. l. limpidus* both survive. The fatal dose of *P. australis* is 1·5 mgm. as compared with 8 mgm. of *C. noxius* or *C. limpidus*.

Next, the cross-effects of the antivenins (prepared from the horse) were compared. The *P. australis* antivenin saved 9 out of 10 mice injected with an otherwise fatal dose of the venom of this scorpion or of *Buthus occitanus*. A boy of 6 years was stung by the latter and in a few minutes became comatose ; he was saved by a subcutaneous injection of 20 cc. of *P. australis* antivenin.

Similar tests with Mexican scorpion antivenins showed that they were much more potent against the Mexican venoms than was *P. australis* antivenin and, *vice versa*, *P. australis* antivenin was much more potent against its own venom than were the Mexican antivenins, although the Mexican venoms were much less toxic than the North African species. With the *C. noxius* venom and Mexican antivenin 31 mice survived out of 50 ; with *P. australis* antivenin only 13 out of 50 ; with *P. australis* venom and Mexican antivenin 25 out of 50, whereas with *P. australis* antivenin " 95 per cent." survived [47–48 out of 50]. There is, therefore, some fundamental difference between the North African and the Mexican scorpion venoms. *H. Harold Scott*

Del Pozo, E. C. Ressemblances et différences dans les actions physiologiques des venins des scorpions. [**Similarities and Differences between the Physiological Actions of Scorpion Venoms.**] *Arch. Inst. Pasteur d'Algérie.* 1949, Mar., v. 27, No. 1, 35–8. [13 refs.]

The author states that the actions of different scorpion venoms are very similar. Injections of large doses of *Centruroides l. limpidus* venom, for example, which is the least toxic of the Mexican scorpion venoms, produce the same effects as the more toxic *C. noxius* and *C. suffusus*. Sergent has shown [see the preceding abstract] that the venoms of *P. australis* and *C. noxius* are antigenically distinct, although, according to the present author, the physiological effects are the same—fibrillation, clonic convulsions, rise of arterial pressure, salivation and paralysis of the movements of respiration. He shows that the muscular movements are due to the action on the motor neurones and not to action on the muscle fibres themselves, for though the convulsive movements are produced by direct contact of the venom on the muscles *if the nerves are intact*, there is no such movement if the nerves to the muscle are severed. The rise of blood pressure is similarly due to the action of the venom

on the spinal cord, on the sympathetic preganglionic neurones of the vessels and the suprarenals. Some organs deprived of their nerve-supply show vaso-constriction which is not seen when the suprarenals are extirpated. The respiratory paralysis is of central origin and is preceded by a long period of irregularity in depth and rate of respiration. Hitherto the interpretations have been varied ; some attributing the effects to peripheral action, others to bulbar, others again to neuro-muscular blocking. *H. Harold Scott*

DERMATOLOGY AND FUNGUS DISEASES

Fox, H. **Cutaneous Manifestations of some Tropical Diseases.** *Arch. Dermat. & Syph.* 1949, Feb., v. 59, No. 2, 127–44, 5 figs.

This is a lecture delivered at the Ninety-seventh Annual Session of the American Medical Association in Chicago in June, 1948.

The author talks of certain tropical diseases with skin lesions which he had met with among soldiers and sailors returned from the late World War. He deals with five only : yaws, pinta, bartonellosis (verruga peruviana), cutaneous leishmaniasis and leprosy. He notes that 32 cases of yaws had been reported from the Army and 24 from the Navy and Marine corps. He does not say how many cases of pinta he has seen, but confines himself to general remarks on the disease and its history. Of oriental sore, 499 cases had been reported from the American Army in the Middle East, probably contracted in Persia. Of Carrión's disease six cases in the Navy and Marine Corps were reported in the war, and of leprosy 22 among veterans. This number is, unfortunately, likely to go up as cases with long incubation declare themselves.

There are excellent photographic reproductions of patients with pinta and verruga. [The paper contains nothing with which readers of this *Bulletin* are not familiar.] *H. Harold Scott*

Guimarães, F. N. & Rodrigues, B. A. O puru-puru da Amazônia (pinta, carate, mal del Pinto etc.). Contribuição ao seu estudo. [**Mal del Pinto in Amazónia, Brazil.**] *Mem. Inst. Oswaldo Cruz.* 1948, Mar., v. 46, No. 1, 135–97, 24 figs. & 1 map. [107 refs.]

Purú-purú, a local name for pinta, or *mal del pinto*, has been given various explanations. One that it was a disease affecting those living on the banks of the Rio Purú ; others that the name is a corruption of " pirú-porú ", itself a corruption of *pirera-poroc*, signifying a " skin which desquamates." The authors give a long list of those who have studied the condition down to the time when Chagas said that it and pinta were one and the same, and investigations in the last 30 or more years have served but to confirm this. They next briefly note the existence of this disease, first outside Amazónia and then in more detail the distribution within the Amazonas, particularly along the rivers Negro, Japurá, Solimões, Javari, Juruá and Purus, and a line map shows this clearly. There follows a detailed description of the clinical features with photographs of patients and photomicrographs of sections of the skin showing the lesions set up. The dyschromic lesions are of three forms : i. Papulo-squamous, with severe itching, and edges well defined ; ii. Maculo-squamous, larger, paler, with at times, pigmented centres ; iii. Dyschromodermic maculae, with pigmentary changes more or less marked, but with little desquamation.

Epidemiological data are based on 69 cases only, hence the facts stated must be accepted guardedly if applied generally. In one district, Labrea, of 28

patients 16 were between 10 and 30 years of age, whereas in another, among 36 patients 18 were between 5 and 15 years. Sex plays no part ; of the 69 there were 34 males, 35 females. As regards race, of the total 24 were blacks, 19 whites, 16 were Indians and 10 were mulattoes. Of 41 in Labrea and Povoado Belém 34 belonged to 8 families [but this might just as easily be explained by a common origin as to a family susceptibility]. The pathological anatomy is well illustrated by tissue sections. The paper concludes with details of 47 cases. Neosalvarsan gave the best results in treatment. *H. Harold Scott*

MASSOUD, G. El D. **The Radiological Picture of Mycetoma. (Report of a Case verified by Biopsy).** *J. Roy. Egyptian Med. Ass.* 1949, Jan., v. 32, No. 1, 64–8.

" 1. A case of mycetoma of the foot is clinically and radiologically described. The diagnosis was ascertained by a biopsy examination.

" 2. At some stages of the disease (not at the start) the radiological picture may suggest the condition. This may be seen in the reported case. The multiple cyst-like areas of bone destruction etc., and the exclusion of pyogenic osteomyelitis, tuberculosis, syphilis, and malignancy suggest a condition of a fungus infection.

" 3. The reported case presents a slight degree of new bone formation ; this is not usual because the common findings in this condition show that it is mainly destructive."

STEWART, C. B. **Histoplasmin Sensitivity in the Maritime Provinces and Newfoundland.** *Canadian J. Pub. Health.* 1949, Apr., v. 40, No. 4, 178–82. [11 refs.]

" 1. Histoplasmin tests were done on 310 Dalhousie University students, most of them males.

" 2. Positive reactions were observed in 4 men (1·3 per cent.), all of whom had been part-time residents of areas outside the Maritime Provinces or Newfoundland.

" 3. No positive reactions were observed in 157 life-time residents of the Maritime Provinces or Newfoundland."

ALLEN, R. M. **Experimental Histoplasmosis : Portal of Entry of the Fungus.** *Amer. J. Trop. Med.* 1948, Nov., v. 28, No. 6, 857–61.

The mode of infection in histoplasmosis is not known, but the frequent occurrence of lesions on the oral mucosa and in the lungs suggests an oral or pulmonary portal. Experimentally, infection is easily achieved by inoculating cultures into susceptible animals by the venous or peritoneal routes, but, apparently, there is no previous record of successful inoculation by the oral or nasal routes.

The author, using living, yeast-form cultures of *Histoplasma capsulatum* attempted to infect guineapigs (12) and mice (30) through the alimentary system by adding suspensions of the fungus to drinking water, and guineapigs alone through the nasal route by introducing the culture suspension through a fine ureteral catheter : for this purpose it was necessary to anaesthetize the guinea-pigs to prevent their struggles. Mice could not be used in this experiment because of their small size. Very large doses of culture were used in all experiments, with the object of obtaining fatal infections.

In the oral feeding experiment, 12 of the 30 mice died in less than 36 days and the remaining 18 were sacrificed between the 23rd and 36th days.

Macroscopic lesions were not shown but the fungus was recovered in culture from the organs of 70 per cent. of the animals. Of the 12 guineapigs in this experiment, 4 died and the remaining 8 were sacrificed: the fungus was cultivated from the organs of 75 per cent. of these animals.

In the nasal experiment, none of the 12 guineapigs died and all were sacrificed at the end of two weeks or later. By culture, 75 per cent. of the animals were found to be infected.

The results of these experiments indicate the possibility of infection by the nasal and alimentary routes. *J. T. Duncan*

NORDEN, A. **Agglutination of Sheep's Erythrocytes sensitized with Histoplasmin.** *Proc. Soc. Exper. Biol. & Med.* 1949, Feb., v. 70, No. 2, 218–20.

SASLAW and CAMPBELL [below] showed that collodion particles in suspension could be sensitized with histoplasmin and agglutinated by a *Histoplasma* antiserum. The present author, following the technique of MIDDLEBROOK and DUBOS (*J. Exper. Med.* 1948, v. 88, 521), used a suspension of sheep erythrocytes in place of the collodion particles. The optimal dilution of histoplasmin for sensitizing the cells was found to be 1 : 2, but undiluted histoplasmin was haemolytic to sheep erythrocytes. A 0·2 per cent. suspension of erythrocytes could be more effectively sensitized than the 0·5 per cent. suspension previously recommended.

Erythrocytes sensitized with histoplasmin were agglutinated by anti-*Histoplasma* rabbit sera but not by anti-*Sporotrichum*, anti-*Candida* or normal rabbit sera. Cross-reactions with anti-*Blastomyces* serum were not attempted.

In recording the tests, a positive result was indicated by the deposition of erythrocytes as a thin adherent film on the hemispherical fundus of the test tube, while a negative result was shown by a flat disc-like deposit of free erythrocytes. The serum end-titre in a positive reaction was as high as 1 : 1,280. *J. T. Duncan*

SASLAW, S. & CAMPBELL, Charlotte C. **A Comparison between Histoplasmin and Blastomycin by the Collodion Agglutination Technique.** *Pub. Health Rep.* Wash. 1949, Mar. 4, v. 64, No. 9, 290–94.

In a previous paper (*Proc. Soc. Exper. Biol. & Med.* 1948, v. 68, 559) the authors showed that a suspension of collodion particles " sensitized " with the soluble antigens of histoplasmin could be agglutinated by a *Histoplasma* antiserum. The present paper is a report of the application of this serological method to the study of the specificity of the *Histoplasma* and *Blastomyces* serum reactions. The degree of sensitizing power varied amongst the different batches of histoplasmin, and for each there was an optimal dilution which achieved the highest degree of sensitization of the collodion particles. The results of the tests showed that *Histoplasma* antiserum could agglutinate histoplasmin-sensitized collodion suspensions up to serum dilutions of about 1 : 160 and 1 : 320, and blastomycin-sensitized suspensions to a lower serum end-titre. The *Blastomyces* antisera were relatively poor in antibody and agglutinated the blastomycin- and histoplasmin-sensitized suspensions only to end-titres of 1 : 10 and 1 : 5 respectively.

So far, the results confirm the earlier findings that an intimate antigenic link exists between *Histoplasma* and *Blastomyces*, evidenced by the cross-agglutination reactions, but the serum end-titres in the homologous systems are higher than those in the heterologous systems. *J. T. Duncan*

Kuzma, J. F. **Histoplasmosis—the Pathologic and Clinical Findings.** *Diseases of the Chest.* 1947, July–Aug., v. 13, No. 4, 338–44. [11 refs.]

Report of a case in Milwaukee, Wisconsin.

Bass, H. E., Schomer, A. & Berke, R. **Coccidioidomycosis. Persistence of Residual Pulmonary Lesions.** *Arch. Intern. Med.* 1948, Dec., v. 82, No. 6, 519–28, 7 figs.

Little is known of the subsequent histories of cases of coccidioidomycosis which have not progressed to the stage of disseminated granulomatous disease and are presumed to have achieved complete recovery. The large number of infections, estimated at 6,000, in the United States Forces during wartime training in the endemic areas of coccidioidomycosis in the south-western part of the United States, has provided abundant material for a " follow-up " investigation. In this connexion, the authors were able to study, in New York city, 20 patients who had " protracted, residual, pulmonary lesions of coccidioidomycosis ", and they give brief summaries of the clinical features of 13 of the cases. Radiography showed pulmonary lesions of various types, *e.g.*, nodular densities, cavities, mottled infiltrations, fibrosis, pleural effusion and calcification. The resemblance of many of the lesions to those of tuberculosis was striking and it is not surprising that the disease had, in several cases, been diagnosed as tuberculosis after the patient's return to civil life. However, these residual lesions characteristically showed no change during a period of observation of from 2 to 5 years. The diagnosis of coccidioidomycosis was based on the following evidence : (*a*), the history of exposure to infection in an endemic area ; (*b*), radiography which showed a pulmonary lesion, usually a solitary cavity or nodular density which remained unchanged during months of observation ; (*c*), indication of an identical lesion in the X-ray picture of the chest at discharge from military service ; (*d*), a positive coccidioidin skin reaction and (*e*), failure to find the tubercle bacillus. Skin sensitivity to coccidioidin tends to diminish with lapse of time and, although a dilution of 1 : 1,000 is usually sufficient to give a strong reaction in an early case, it was necessary to use the reagent at 1 : 100 or even 1 : 10 in the residual cases. The reactions, also, were rather weak in contrast with the strong reactions given by early cases. Despite the pulmonary lesions described, all of the patients were asymptomatic except three : one being a patient with cavity and recurrent haemoptyses, another with pleural effusion and the third with a progressively disseminating disease. In the cases with cavity, there was no evidence of bronchogenic spread or of seeding to other parts of the lung fields, such as occurs commonly in tuberculosis. *J. T. Duncan*

HEAT STROKE AND ALLIED CONDITIONS

O'Brien, J. P. **Tropical Anhidrotic Asthenia : its Definition and Relationship to other Heat Disorders.** *Arch. Intern. Med.* 1948, June, v. 81, No. 6, 799–831, 1 fig. [Refs. in footnotes.]

Until recent times little has been known of the ill-effects which may be due to increasing impairment of sweat function arising during residence in tropical countries where miliaria rubra (prickly heat) is of common occurrence.

The disorder called tropical anhidrotic asthenia is characterized by exhaustion, headache and dyspnoea associated with failure of sweating over a large area of

the body when working in the heat. Sweating may be profuse on the face but markedly diminished over those covered areas of the body where prickly heat is most commonly found. The condition is held to be due to the occlusion of the sweat ducts and the extravasation of sweat into the tissues. The paper contains a very full discussion of symptoms and signs. Details of 38 severe cases are compared with those given by other workers, in particular the cases of heat exhaustion type 2 described by LADELL *et al.* in Iraq [this *Bulletin*, 1945, v. 42, 143].

The question of terminology for this disability due to post-miliarial obstructive impairment of sweat function, as distinct from the classic heat disorders, is considered in some detail. It is thought that the development of this disorder constitutes a specific form of tropical deterioration which limits the duration of an individual's acclimatization to residence in the tropics. *G. P. Crowden*

TROPICAL ULCER

ADAMSON, P. B. **Tropical Ulcer in British Somaliland.** *J. Trop. Med. & Hyg.* 1949, Apr., v. 52, No. 4, 68–76. [19 refs.]

The author considers that present data show that tropical ulcers are probably caused by " Vincent's fuso-spirochaetes in a host who has become susceptible to infection as a result of vitamin-B deficiency and possibly further debilitated by chronic disease and malnutrition " [BLANK, this *Bulletin*, 1947, v. 44, 935]. Tropical ulcers occur in Somaliland throughout the country, from the cold highlands of Erigavo to the hot and moist areas around Berbera.

In 1947, out of a total of 7,737 in-patients, 999 were treated for this condition (135 being women), an unexplained feature being the relative infrequency in women as compared with men. It is probable that patients only attend a European doctor when the ulcers are very severe, or where a proper hospital lies within a convenient distance. A large number of early cases are probably attend d by local practitioners, who are of the Midgan (sweeper) class. In treatment by these Midgan, the ulcer is cleansed as well as possible with a rag or other material, powdered bark of an unidentified Acanthus (Glover), called in Somali the *lalis* tree, is made into a thick paste or applied dry, and the whole area covered by a layer of mud which is left in position until it drops off or the patient decides to remove it. Alternatively, powdered white catkins from *Aerva tormentosa*, Forsk, are used. In a personal statement to the author it was claimed that *lalis* bark cured 50 per cent. of ulcers, the time taken for cure not being stated.

Investigations were carried out at Hargeisa, a series of 114 cases being examined before the April rains in 1948. Fifty-three unselected cases were admitted to hospital, one group of 26 patients being put on normal hospital diet [which is described in detail], rest in bed and local treatment (application of eusol dressings followed by 1/1000 acriflavine daily), the second group of 27 patients receiving ascorbic acid tablets, 103·75 mgm. daily by mouth, in addition. One hundred and ten patients had a complete blood examination, including reticulocyte count and blood sedimentation rate and blood films for malaria : routine urine examination was also made. Kahn tests and vitamin-C-estimations of plasma were done, and all in-patients had a routine stool examination on admission. One hundred and forty-nine controls were examined for plasma vitamin-C content before the April (*Gu*) rains, and in all of them, the level was found to be above that in patients with tropical ulcers (average for controls 1·55 mgm. per cent. and in ulcer patients 1·065 mgm. per cent.).

The author draws the following conclusions :—

1. Trauma was an almost constant predisposing factor.

2. No cases of tropical ulcer in females were found at Hargeisa during the period of investigations (February to July, 1948). The poorer classes were more likely to be affected than the richer ones. Age was unimportant except that very young children seemed to be exempt.

3. Associated diseases were not significant except to lower the general resistance, and the anaemia present was considered to be merely a nutritional defect. The Kahn test may be positive in tropical ulcer.

4. There was a diminution in the plasma level of vitamin C in cases of tropical ulcer, but oral vitamin C (ascorbic acid) was of no specific use. Reticulocytosis and raised blood sedimentation rates occurred.

5. In 10 per cent. of cases there was a periostitis or bone necrosis which delayed healing, and it is considered that the fusiform bacilli are responsible for this condition.

6. The most sensitive indicators as regards prognosis were the smears from ulcers and plasma vitamin C levels : the blood sedimentation rate and reticulocyte count were also useful guides.

7. Hospital diet was considered to be below the optimum standard and should be adjusted to a higher level of vitamin C, while protein may be required to be increased. At present the only source of vitamin C is camel's milk. Officially each patient receives a pint of milk daily, but in practice usually a good deal less was available. After the rains have begun the vitamin C content of camel's milk averages 2·698 mgm. per 100 ml.

[For details and results of the various laboratory investigations the reader is referred to the original paper.] *C. F. Shelton*

Magara, M., Go, K., So, K. & Akima, T. **On a New Species of Anaerobic Coccus isolated from Tropical Ulcer.** *Japanese Med. J.* 1948, Aug., v. 1, No. 4, 289–91, 2 figs.

From 19 specimens from tropical ulcers, the authors, in Japan, isolated an anaerobic coccus from ten. It was also isolated from two ulcers produced experimentally by inoculation of secretion of tropical ulcers into other persons. The coccus was isolated more frequently in the early stages : subsequently, it was possible to isolate it from almost every case.

The organism is a Gram-positive non-motile, non-sporing coccus, usually appearing in diplococcus form and having a diameter of about 1·5 to 1·8 μ. It is strictly anaerobic. The cultural characters are given in detail and they suggest, as the authors point out, that the character of the diplococcus resembles that of *Diplococcus magnus* (Tissier and Martelly), but differs from it in producing black pigment in culture on " Vf bouillon with liver pieces " and also in being pathogenic to animals. Broth cultures injected intradermally into rabbits and guineapigs produced ecthyma and from the resulting abscesses, the diplococcus was found in pure culture.

Serologically, the coccus was agglutinated both by patients' serum and normal serum.

In 143 strains of cocci isolated from the female genitals and oral cavity, only 1 strain of *Diplococcus magnus* was found and no cocci identical with the diplococcus now described were found.

The authors suggest that the diplococcus is rarely found except in tropical ulcer : and since spirochaetes and fusiform bacilli are not confined to tropical ulcer, it is suggested that this diplococcus is the essential cause of tropical ulcer. They have therefore named it *Diplococcus tropicus*. [This interesting

observation merits further investigation: but in view of the small series of cases and the inconclusive serological findings, the basis for giving the organism this specific name is perhaps a little uncertain.] *H. J. O'D. Burke-Gaffney*

VAN ZANTEN, T. V. Beenverlenging bij het ulcus tropicum. [**Elongation of the Leg in Tropical Ulcer.**] *Nederl. Tijdschr. v. Geneesk.* 1949, Feb. 5, v. 93 (i), No. 6, 408–9.

The English summary appended to the paper is as follows:—

" In sufferers from low-seated ulcera tropica, the leg is often elongated. The cause is not clear. The author expects the phenomenon to disappear on the availability of better nutrition and better medical care."

HALAWANI, A. **Desert, Septic, or Veldt Sore in Egypt.** *J. Roy. Egyptian Med. Ass.* 1944, Aug., v. 27, No. 8, 214–36. [19 refs.] [Recd. 13 Dec., 1948.]

During 1943 and 1944 there were outbreaks of ulcer in several towns in Egypt, including Port Said and the author saw approximately 500 cases. They were of the type usually called septic, desert or veldt; some were very septic and assumed a phagedaenic character. The former were " punched out and circular in outline with undermined edges and thickened margins ", whereas the more septic cases were progressive and showed finger-like extensions and often exposed underlying bone.

C. diphtheriae was isolated in 7 out of 32 cases, but, as in many cases the ulcers had already been swabbed with formalin, it is believed that this was the main causal organism. Staphylococci, streptococci, *Proteus*, *P. pyocyanea*, spore-bearers, and fusiform bacilli, the last-named in 4 of 60 cases, were also isolated.

An ulcer was produced in a guineapig by inoculating *C. diphtheriae* into the flank with a small dose of antitoxin into the peritoneum at the same time, and in an Egyptian hedgehog (*Erinaceus auritus*) an ulcer was produced by inoculating material from a case showing fusiform bacilli, but attempts to produce ulcers in animals by inoculating other micro-organisms were unsuccessful.

The author believes that malnutrition is a predisposing factor. Most patients were on a poor diet deficient in protein, vitamin A, nicotinic acid, and riboflavin. The vitamin-A content of the blood was always very low. Serum calcium and blood urea were within normal limits, but the blood sugar was often low and curves flat.

Syphilis was a commonly associated infection and the Wassermann reaction was positive in 28·5 per cent. of cases.

Nutritional defects were corrected and concomitant diseases treated; diphtheria antitoxin was given where indicated; and sulphanilamide powder was applied. Some dramatic results were obtained with the last named. The popular formalin-swab method was also used. The ulcers are cleaned up quickly by this method but their duration was not cut short; this is a very cheap form of treatment. *L. E. Napier*

MISCELLANEOUS DISEASES

LAMPRELL, B. A. **Tropical Neurasthenia.** *Med. J. Malaya.* 1948, Sept., v. 3, No. 1, 34–40.

The author during a long tropical service has seen a distressing number of cases of tropical neurasthenia including a number that ended in suicide.

The condition is common in Malaya of which he is writing. In a group of rubber plantations with an average staff of 75 (presumably Europeans) in the past two years, one has committed suicide, eight have been repatriated for nervous breakdown, and two have been sent on home leave for the same reason. In a series of 33 invalidings analysed by SQUIRES [no reference given] 45 per cent. [15] were for psychological reasons.

Neurasthenia in the tropics differs from that seen in practice in temperate countries by the predominance of cerebral over spinal symptoms. The mild cases show increased irritability with occasional outbursts of uncon rolled rages, restlessness, and moderate amnesia. In the intermediate cases these symptoms are worse and periods of worry and depression occur, often amounting to delusions of persecution with insomnia. In the severe cases, the depression is predominant ; to this is added procrastination and indecision, loss of confidence, fear of insanity and of loss of employment, which constitute a vicious cycle that may end in suicide.

The author classes the causes as personal and environmental, the former being the more important ; the prominence of the personal factor is due to the tendency for social misfits and others who are dissatisfied with home conditions to seek employment in the tropics where they hope to find life easier. The environmental factors are (i) Exile from one's own country and loss of firm roots in a place that one calls home. (ii) The excessive stimuli of the tropics ; under this heading the author includes the direct effects of the climate and discusses the sexual factor. (iii) Overwork and excessive responsibility. (iv) Isolation and monotony ; under this last heading [the sequence of thought is obscure to the reviewer] he includes a suggestion that the recent increased rate of breakdown in Malaya may be due to years of war strain and present economic and political difficulties.

The preventive measures he advocates include more careful selection of candidates for service in the tropics and the suggestion that a psychiatric assessment as well as a physical examination should be made ; more frequent home leave ; annual local leave to a hill station ; shorter office hours ; more security of tenure of appointments in commercial undertakings ; and freedom to marry early in his service. Finally, the author suggests that, since this problem is an admittedly serious one, the Malayan branch of the British Medical Association should make a study of its aetiology and prevention, and convey their conclusions to the Government and to commercial and industrial associations. *L. E. Napier*

GARCIA CARRILLO, E. El corazón en relación con algunas enfermedades tropicales. [**The Heart in certain Tropical Diseases.**] *Rev. Med. Costa Rica.* 1948, Aug., v. 15, No. 172, 193–6. [20 refs.]

A short review of the literature.

VINT, F. W. **Some Observations on the Anterior Lobe of the Pituitary Gland in the Adult Male African.** *East African Med. J.* 1949, Mar., v. 26, No. 3, 58–68.

AYYAR, S. R. **Eosinophilic Lung.** *Indian Med. Gaz.* 1948, Dec., v. 83, No. 12, 551–2.

An account of 24 cases, treated with either mapharside or acetylarsan, with satisfactory results.

Théodoridès, J. Les coléoptères parasites accidentels de l'homme. [**Accidental Infestation of Man by Beetles.**] *Ann. Parasit. Humaine et Comparée.* 1948, v. 23, Nos. 5/6, 348–63. [39 refs.]

Beetles or their larvae are sometimes recorded as having been taken from some part of the human body. Their presence is accidental as they are not parasitic on man. In a brief review of the published records the cases are grouped according to the site of infestation : (1) the digestive system ; (2) the ear, nose and eye ; and (3) the genito-urinary system.

A table is given summarizing the data concerning sixteen species.

H. S. Leeson

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

Congo Belge. Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge. Rapport sur l'Activité durant les années 1946 et 1947 [de Brauwere, P.]. [**Report of the Activities of Foréami during 1946 and 1947.**] 140 pp., 3 maps & 3 diagrams. [Recd. 1949.] Brussels : 112 Rue du Commerce.

The war-time experiences of the excellent Belgian organization Foréami were reviewed in the Report for the years 1939 to 1945 [this *Bulletin*, 1948, v. 45, 816], which also sets out the general pattern of its organization. The present report covers the early stages of recovery and the preparation of plans for expansion. Work originally started in extremely unhealthy areas of the District of Kwango is now being stabilized in that district and in small areas of the Districts of Moyen-Congo and Lac Leopold II, divided into six sub-sectors with a total population of 624,600 people. The work includes the taking of an original census of the whole population, the medical examination of every person in his home, reinforced where necessary by laboratory procedures, and the preparation of a medical card for each. Each year the census is revised and as high a proportion as possible of the medical examinations repeated, 86 and 88 per cent. having been re-examined in the years under review. In this way exceptionally valuable data are collected on the prevalence and social importance of different diseases, and on demographic happenings. In association with this survey the sick are treated either locally or by despatch to a hospital centre, public health education is carried out, and both general and special sanitary measures are instituted. The sick who report for treatment independently of their discovery in a survey process are also treated and constitute the bulk of patients.

The organization has now passed through its infancy. Much has been learnt by the survey process and public confidence has so increased that there is little remaining need to search for the sick. In the process of stabilization the survey will recede from its position of paramount importance to one of secondary importance in comparison with medical treatment and the improvement of health. The old dispensaries, once a local marvel, are now giving place to fully equipped hospitals in each sub-sector, served by more elaborate rural dispensaries which have themselves some of the characters of hospitals, and staff are being transferred from survey to strictly clinical duties.

The commonest causes of morbidity and mortality are diseases of the respiratory and alimentary systems, with nutritional conditions running them close. There was a remarkable absence of epidemic disease, the sole one worthy of notice being an outbreak of amoebic dysentery which proved unusually resistant to specific treatment [the statement that chiniofon "*semble être un*

médicament de premier ordre" in the treatment of this disease is not borne out by the data given]. The state of the major endemic diseases is less satisfactory, though trypanosomiasis [reviewed separately in this *Bulletin*, 1949, Oct., v. 46] has greatly decreased, malaria remains a scourge demanding control by all possible means, while the helminthiases and nutritional deficiency diseases remain of the greatest importance. Yaws, of which 752 new and 145 old cases were seen, has sunk to a position of minor importance though previously extremely common, and fortunately the incidence of tertiary cases reflects the present, rather than the past, incidence of primary cases. Leprosy remains common, 0·24 per cent. of the population being affected, and the standard methods of control by voluntary or compulsory isolation, which have failed, are now being replaced by the establishment of a model village with a high standard of amenities to which patients will be attracted by treatment with the new drugs. Tuberculosis is a serious problem, to combat which the five-year plan proposes to institute BCG vaccination, mass miniature radiography, and a model sanatorium. Venereal diseases are not very common. Helminthic infections are universal, ankylostomiasis being the commonest, but the author makes refreshing comments on the excessive readiness of practitioners to attribute illness to this cause when others are responsible. Among all these various causes of sickness, however, the author focuses attention on the importance of malaria, which practitioners tend to regard as a mild disease but which he considers enhances the infant mortality in the absence of prophylactic treatment by about 150 per thousand. Against malaria Foréami is instituting a control system based on house-spraying [the insecticide is not stated, but pyrethrum can be inferred], and on the wide use of prophylactic paludrine and chloroquine.

Demographic data are fully tabulated. During the war the birth rate dropped and though there was no marked increase in mortality other than the infantile mortality the population actually decreased in some areas. The position is now fully restored and the death rate is lower than any previously recorded. The following basic statistics for 1947 are either directly given or can be deduced from the tables :—birth rate 41·24 per 1,000, crude death rate 25·75, natural increase 15·49, infant mortality rate 88·4 per 1,000 births, fertility rate 176 and net female reproductive rate 1·3. The age distribution of the population, and the mortality per 1,000 in each age group in 1947 were :—

Age	Percentage of population in the group	Mortality per 1,000 per year
0–3...	11·1	74·4
3–15 [*sic*] [?4–14]	39·7	15·0
15–45 [?15–44] ...	42·6	19·2
45 and over ...	6·6	62·0

The death rates by age groups are very high, roughly double those of India, their nature being obscured in the crude death rate by the abnormally young age constitution of the population. Nevertheless the high fertility rate balances them and, if this state continued, the population would be a rapidly growing one. [The reviewer is sceptical about the accuracy of the infant mortality rate, which does not tally with the mortality in the 0 to 3 group, but accepts the other figures as at least a good approximation. The data given are unique for tropical Africa.]

The report concludes with notes on experimental work on paludrine and chloroquine prophylaxis, and on the incidence of filarial infection.

[For earlier accounts of the organization of Foréami, see TROLLI, this *Bulletin*, 1940, v. 37, 521, and HUMPHRIES, *ibid.*, 523.] *G. Macdonald*

INDIA. **Annual Report of the Malaria Institute of India for the Year 1947** [SINGH, J., Director]. 19 pp. 1948. Delhi: Manager of Publications, Civil Lines.

The Malaria Institute of India reports a successful year's work in 1947 despite the need for its staff to undertake much emergency work necessitated by refugee movements. Work must also have been impeded by several changes of staff exemplified by the fact that three Directors during the year are named.

Courses of instruction continued on a normal basis and a special one for engineers has now been standardized. Many papers have been published, and interesting points in the research programme deal with laboratory trials of the prophylactic value of Cam-Aqi and resochin (chloroquin) against *Plasmodium knowlesi*, in which Cam-Aqi given in doses of 20 mgm. daily for one week subsequent to inoculation proved effective in two monkeys. Field trials with paludrine showed it to be a highly effective therapeutic agent under Indian conditions, 0·1 to 0·3 gm. effecting a clinical cure in most cases, and a prophylactic trial in which three dose regimens, approximating 300 mgm. once a week, were employed was very successful. The notable feature of the work is the increasing amount of responsibility for routine malaria control in the Province of Delhi, in Coorg and in the coalfields. *G. Macdonald*

HINMAN, E. H. **The National Malaria Society : Past, Present, and Future.** *J. National Malaria Soc.* 1949, Mar., v. 8, No. 1, 1–13, 1 fig.

The National Malaria Society owes its origin to a resolution at the Pan-American Scientific Congress in 1916 which led to the formation of a Committee, whose objectives were : (*a*) to stimulate interest in malaria problems ; (*b*) to serve as a medium through which societies and individuals might become identified with the study and prevention of the disease ; and (*c*) to co-ordinate the efforts of these agencies with constituted Federal, State, and local authorities. Until 1941 the Committee had an extremely varied career and was only successfully maintained through the activities of a few enthusiastic persons. In 1941, however, its constitution was radically changed and the National Malaria Society was formed in the place of the previous Committee, the Society undertaking the publication of the *Journal* which has now become well known.

With this change the Society has steadily prospered and undertaken much work in the co-ordination of malaria control activities both for the armed forces and the civilian authorities. In reviewing future prospects its officers foresee the possibility of its disintegration on the unique grounds that its objects may shortly be completely fulfilled by the disappearance of malaria from the United States. In this paper the writer reviews its place and considers the possibility of fusion with a society interested more generally in tropical medicine, following the example of the International Congresses. [Considering its recent successful career and the value of the *Journal* the arguments would seem to be strongly in favour of continued existence with interests extended from the United States to the tropical world.] *G. Macdonald*

SHANGHAI. Rapport sur le fonctionnement technique de l'Institut Pasteur de Chang-Hai en 1948 [FOURNIER, J., Director]. [**Annual Report of the Pasteur Institute, Shanghai, for the Year 1948.**] 46 pp., 1 fig. 1949.

The first of the five parts into which this Report is divided deals with general laboratory investigations. Routine examinations are shown in detail in tabular

form. In all, there were 15,438 medical and 681 veterinary investigations. The former included 2,443 parasitological and 3,084 serological examinations. It is noted that only 22 of 152 blood films contained malaria parasites (15 *P. vivax*, 6 *P. falciparum* and 1 *P. malariae*). *Entamoeba histolytica* was present in only 8 of 710 stools. The commonest helminthic ova found were those of *Ascaris* (126) and *Trichuris* (130). *S. japonicum* ova were found 5 times.

A section of this part deals in some detail with salmonellosis and the bacteriology of summer diarrhoea. Of 1,054 patients, 227 gave positive results in one or more tests for *Salmonella* infection. Of these positive results, 65 per cent. were due to *Salm. typhi.*, 14 per cent. to *Salm. paratyphi B*, and 11 per cent. to *Salm. paratyphi A*. There were also recorded 4 per cent. of group C and 6 per cent. of " other salmonellae ".

Isolations from different materials included 14 species of *Salmonella* and 4 unidentified strains. From 145 strains, *Salm. typhi* accounted for 82, *Salm. paratyphi B* for 28 and *Salm. paratyphi A* for 16. None of the other species exceeded 3.

It is stated that 70 per cent. of the isolations from summer diarrhoea were of *Shigella* organisms of which 61 out of 92 were of the *Sh. flexneri* II type. *Sh. shigae* was only found once (in a severe case of dysentery) as was *Sh. sonnei*.

The second part of the report deals with the anti-rabies Institute. Full statistical details are given. In 47 cases the biting animal was proved to be infected by laboratory tests and in 80 it was clinically rabid. In all, 933 persons were treated (456 with complete courses). There were no deaths and no paralytic accidents. During the year, some 80,000 cc. of phenolized vaccine were prepared and also 28,000 cc. of formolized vaccine for veterinary use.

Points of special interest were (1) a case in which Negri bodies were absent in a dog's brain which was proved to be infected by inoculation tests. This is the first time since the service began in 1942 that the two diagnostic methods did not agree. (2) Three cats were found to be positive—a higher figure than in previous years. (3) The saliva of a human being with rabies was found to be infective for rabbits.

The third part of the report records the BCG service. In 1948, 22,248 cc. of oral vaccine were issued compared with 4,354 in 1947. Parenteral vaccination was used in the form of intradermal inoculation (0·04 mgm.) or scarification (20 to 25 or 75 mgm. per cc.). It is stated that no complication followed scarification, but the intradermal method often resulted in the formation of a cold abscess at the site of inoculation. In one such case, a strain of BCG from the abscess was isolated on Sauton medium, but it was not pathogenic to guineapigs.

The fourth part gives an impressive list of the large number of vaccines and other biological products produced or stocked in the Institute, and the last part describes various missions, conferences and publications relating to members of the staff. *H. J. O'D. Burke-Gaffney*

BOOK REVIEW

HAYAKAWA, Kiyosi [M.D., Ph.D.]. **A Comparative Study of Japanese and Tropical (Scrub Typhus) Tsutsugamushi Disease** (*R. orientalis* **var.** *tropica*). 1946, Feb. 13, 66 mimeographed pp., 56 photographs & 15 charts. [45 refs.] Scrub Typhus Research Unit, Institute for Medical Research, Kuala Lumpur.

This interesting report, written in impeccable English by the author, deals with studies carried out by him during the war while he was Assistant Director

of the Japanese Army Institute for Preventive Medicine at Singapore. The substance of the paper has been published in Japanese in the *Journal of the Niigata Medical Association*, 1946, v. 60, 274.

The author has reached the conclusion that tsutsugamushi disease in the tropics differs from the Japanese form in being of lower virulence, so he proposes the name *Rickettsia orientalis* var. *tropica* for the causative agent and the name tropical tsutsugamushi disease to replace such names as tropical typhus, Sumatra mite fever, and pseudo-typhus. [As the paper is written in English the last-named title should be pseudo-typhoid which is the correct translation of the German name "*pseudo typhus*" and is the name employed by Schüffner himself in his papers in English on the disease; for example the paper by him quoted in the present report which appeared in the *Philippine Journal of Science*, 1915, v. 10, 345, is entitled "Pseudo-typhoid Fever in Deli, Sumatra."]

After a close and prolonged study of tsutsugamushi disease in the Japanese-occupied areas of the tropics, the author believes that it differs from the Japanese form chiefly in the following respects:—(1) the incubation period is longer, "more than 15 days"; he bases this opinion on two small groups of cases in one of which 25 patients had been exposed to the risk of infection over a period of 11 days and the first attack occurred 15 days after the end of the period; in another smaller group the first attack occurred 16 days after entering the infected area, and as the patients appear to have remained in the area till the onset of their illness there is no justification for estimating the period "roughly as counting from the date of their arrival." [There is abundant evidence from many reliable sources that the incubation period of scrub typhus is much shorter on the average than 15 days; for example in the dramatic outbreak in Ceylon in which 756 cases occurred after field exercises by British troops between the 11th and 15th December, 1943, patients were being admitted to hospital "by the hundred" as early as the 22nd December.] (2) The initial ulcer was usually absent in the tropical type, though it was detected by the author in 14 out of 17 patients seen by him in Singapore. (3) Leucopenia is more consistently observed in Japan, but the only white cell counts recorded in the paper deal with a group of 16 British prisoners in Singapore, and among these they were less than 5,000 per cmm. in three, and less than 6,000 in two others; the day of the disease is not stated. (4) The case mortality was lower in the tropical form; usually less than 5 per cent.

Fifteen strains of rickettsiae isolated in the tropics were investigated by the usual methods and compared with two strains obtained from Japan; "rather constant" differences in virulence were found; the most significant being that the tropical strains did not completely immunize monkeys against challenge by the Japanese strains, whereas the Japanese strains completely immunized the animals against the tropical strains. A significant statement is that one of the Japanese strains, after being maintained in the tropics by mouse passage for more than 18 months, had lost so much of its virulence that it "now rather resembles the tropical strains."

Admittedly all the differences were quantitative rather than qualitative, and in view of the pronounced differences observed by western workers as occurring among the Far-Eastern strains of *R. orientalis* the author's proposal to recognize tropical tsutsugamushi disease as a distinct variety is not likely to meet with general acceptance.

The author describes an extensive study of the transmitting vectors and the wild rats on which they were found. *R. orientalis* was isolated from larval *Trombicula deliensis* and their rat hosts. About 18 per cent. of the rats caught both in infected and uninfected areas in the Singapore region gave positive Weil-Felix reactions with *Proteus OXK*.

T. akamushi was not found in Malaya, Sumatra, Java, or the Philippines, and so was regarded as not being a vector of the tropical variety of the disease. [But Col. Audy, to whom we are indebted for the copy of the report, states that *T. akamushi* is common in Selangor where it, as well as *T. deliensis*, is definitely a local vector: he also states that the Japanese had many more cases of scrub typhus than are mentioned in the report; for example several thousand cases in Upper Burma, whereas the only important outbreaks listed by the author are as follows:—Kabanjar, Sumatra (80 cases in April, 1943); North Irrawaddy River bank (several hundred cases in October, 1943); Atjeh, Sumatra, and Phuket, Siam (more than 100 in each, in December, 1944).]

At first the disease was not recognized, it was called "Tenta" (bushy swamp) fever. In October 1943 a rickettsia was first isolated from a patient by K. TAISE, who described the disease as an "unknown fever", but the strain when examined by the author at Singapore in February 1944, was found to be *R. orientalis*. Even then, the Japanese doctors who had seen tsutsugamushi disease in Japan believed that they were dealing with a different disease; they regarded the presence of an initial ulcer as an essential feature of the Japanese disease.

The author has carried out a remarkably thorough investigation which does him credit, even though the chief importance of the experience of the Japanese medical men in connexion with scrub typhus is to serve as a striking example of the misconceptions that result from failure to recognize the wide range of variability of the disease. *John W. D. Megaw*

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